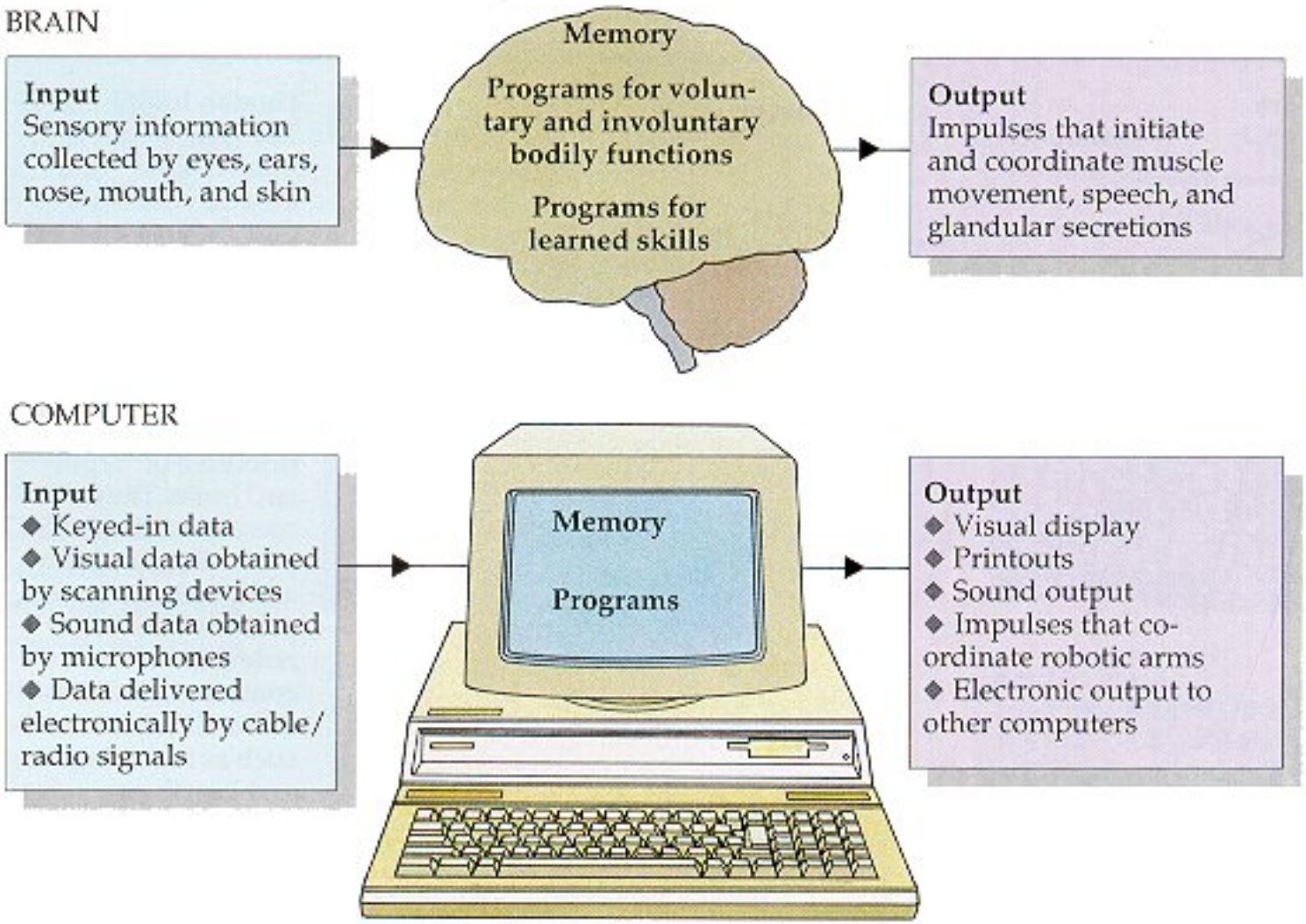
Nervous System

IS THE BRAIN LIKE A COMPUTER?



Brains and supercomputers

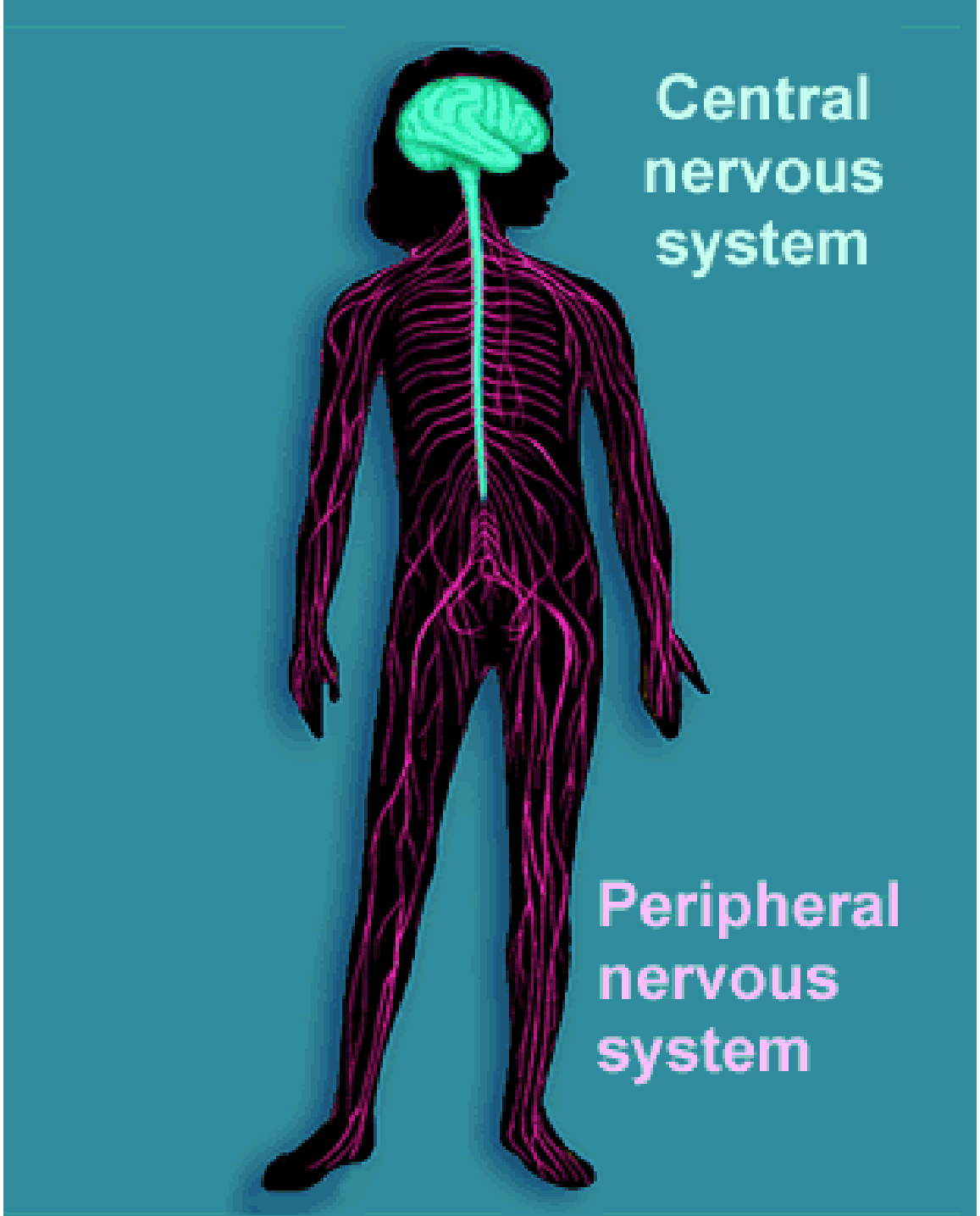
One of the most remarkable aspects of your brain is its ability to "run" several programs at once. For example, it can simultaneously control body temperature, coordinate walking movements and speech, and engage in thought. To approach your brain's level of performance, separate computers or sections of computers would have to be operated simultaneously, with numerous interconnections. Your brain also outperforms a computer at certain specific skills, such as recognizing connections between apparently unconnected ideas and identifying whole objects from only a small part.

Functions

- Regulates internal body metabolism (internal environment)
  - body temp, urine volume, blood volume, gas exchange, circulation, movement
- Llnk to the external environment- (interpreter)
  - sensory devices- sight, hearing, taste, smell, touch (pressure, pain, hot, cold)
  - emotional response to external stimuli (these drive desire to satisfy physical needs to preserve homeostasis)
    - hunger, thirst, temperature, rest, sexuality

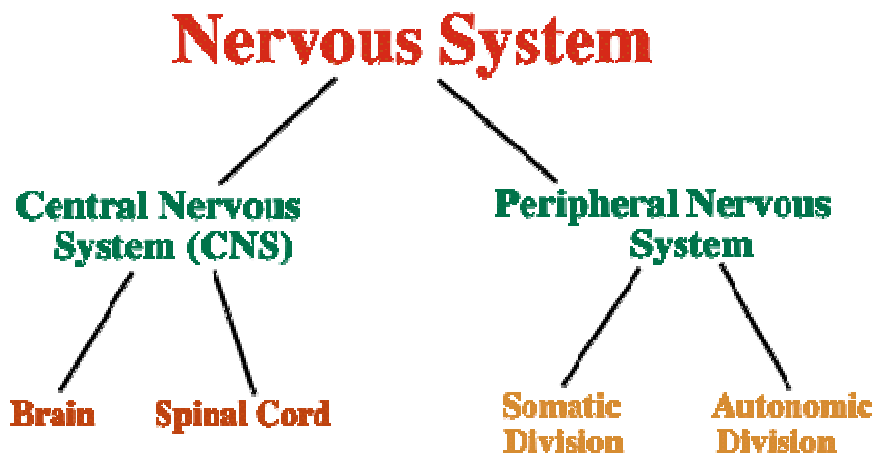
The Two Types of Neural Pathways

- **Sensory** (afferent) nerves transmit messages from sensors to CNS
  - sensory receptors located the ends of peripheral nerves that **detect external and internal environmental changes and relays info to brain**
    - light and sound intensity
    - touch- changes in skin pressure
    - temperature variation
    - oxygen concentration in fluids of the body
  - **impulses** are brought to CNS where they are **integrated to create sensations**
  - Conscious or subconscious decisions are made and acted upon by motor functions
- **Motor** (efferent)- nerves transmit messages from CNS to effectors
  - muscles that contract
  - glands that secrete


Central nervous system
Peripheral nervous system

Nervous Tissue

- **Central-** consist of the brain and the spinal cord
  - incoming sensory signals from PNS travel to the CNS for processing
  - out going signals to from CNS to PNS
- **Peripheral-** connects the sensory receptors,glands, and muscles in the peripheral part of the body to the CNS



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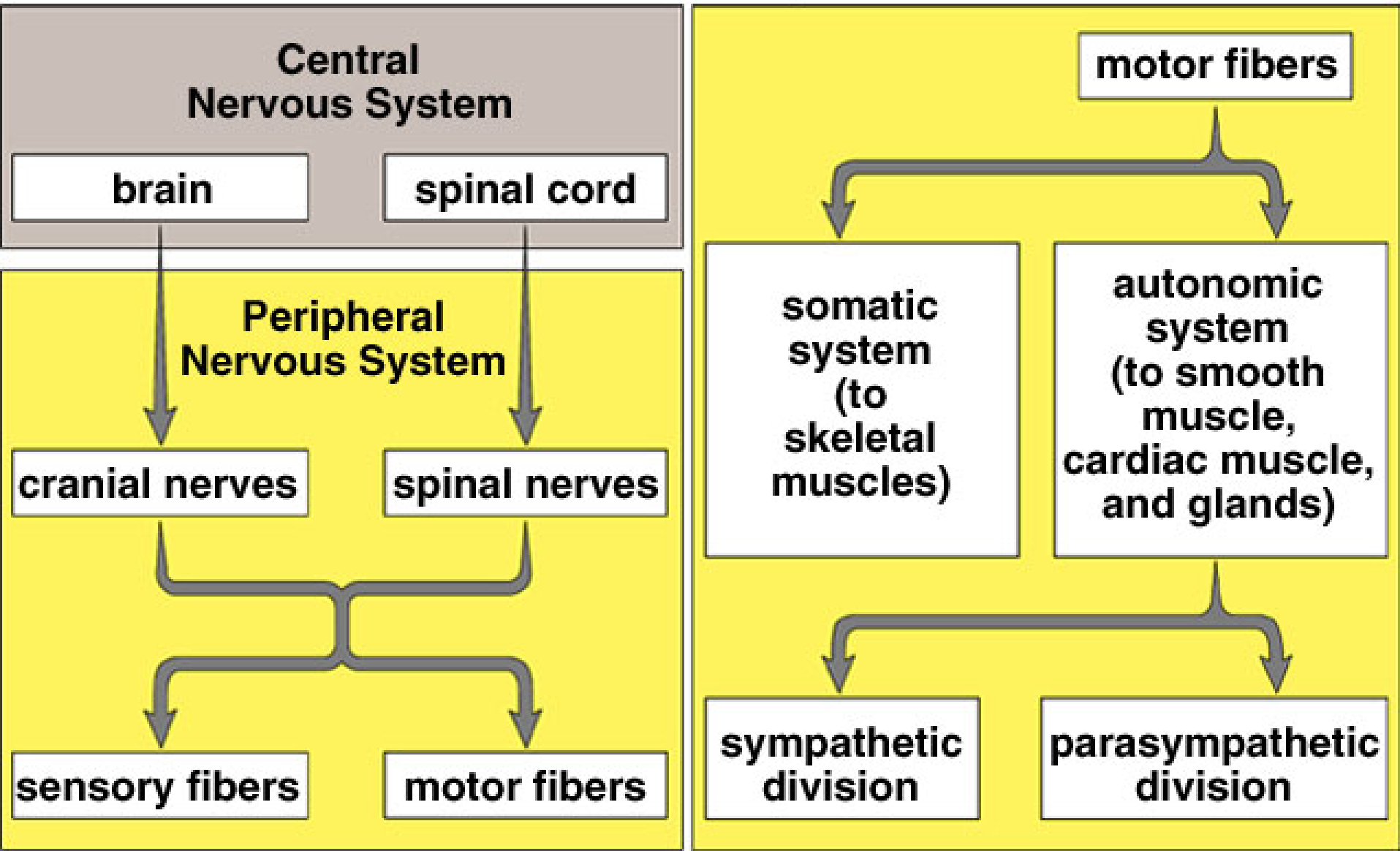
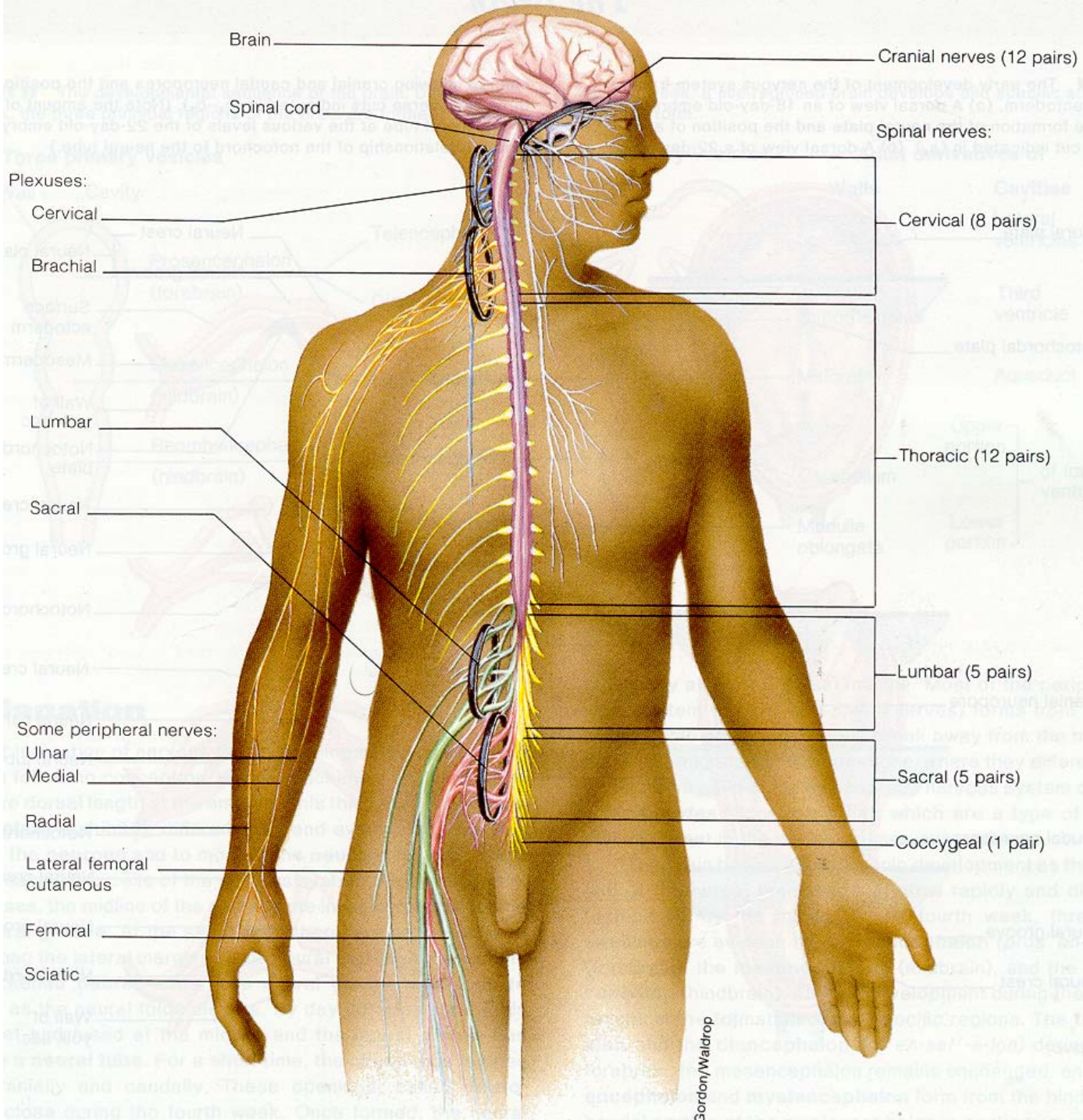
Organization of the Nervous System



Peripheral NS

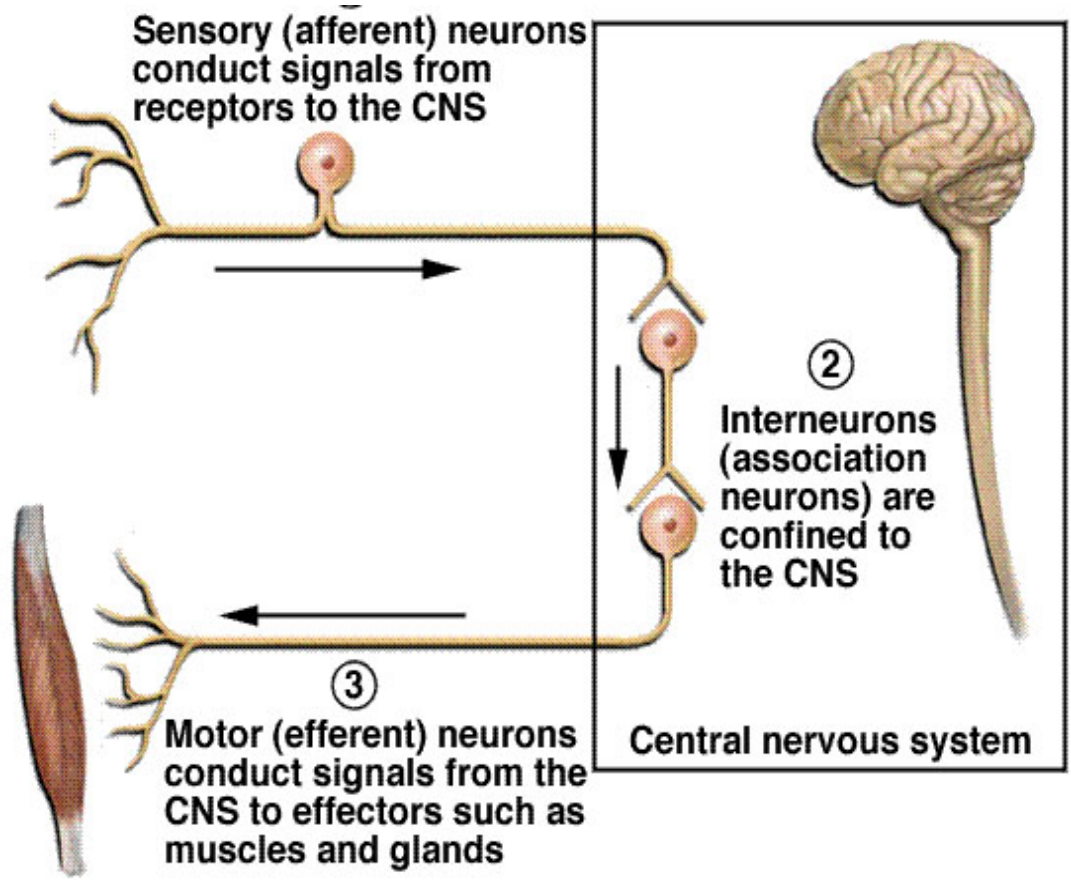
- consist of the **cranial nerves** (derived from the brain) and the
- **spinal nerves** (emerge from the spinal cord).



Peripheral Nervous System

Types of Neurons

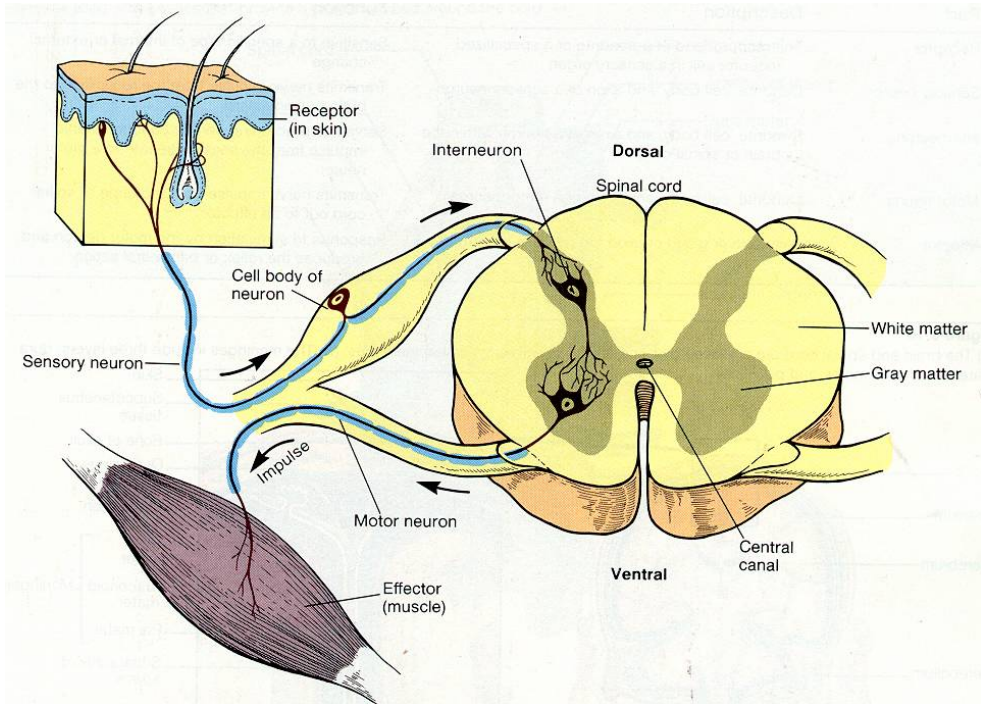
- Input components consist of **sensory (afferent)** neurons.
- The output component consist of motor (**efferent**) neurons.
- **Interneurons** (association) neurons carry nerve impulses from sensory to motor neurons and are located in the CNS.


Sensory (afferent) neurons conduct signals from receptors to the CNS
②
Interneurons (association neurons) are confined to the CNS
③
Motor (efferent) neurons conduct signals from the CNS to effectors such as muscles and glands
Central nervous system

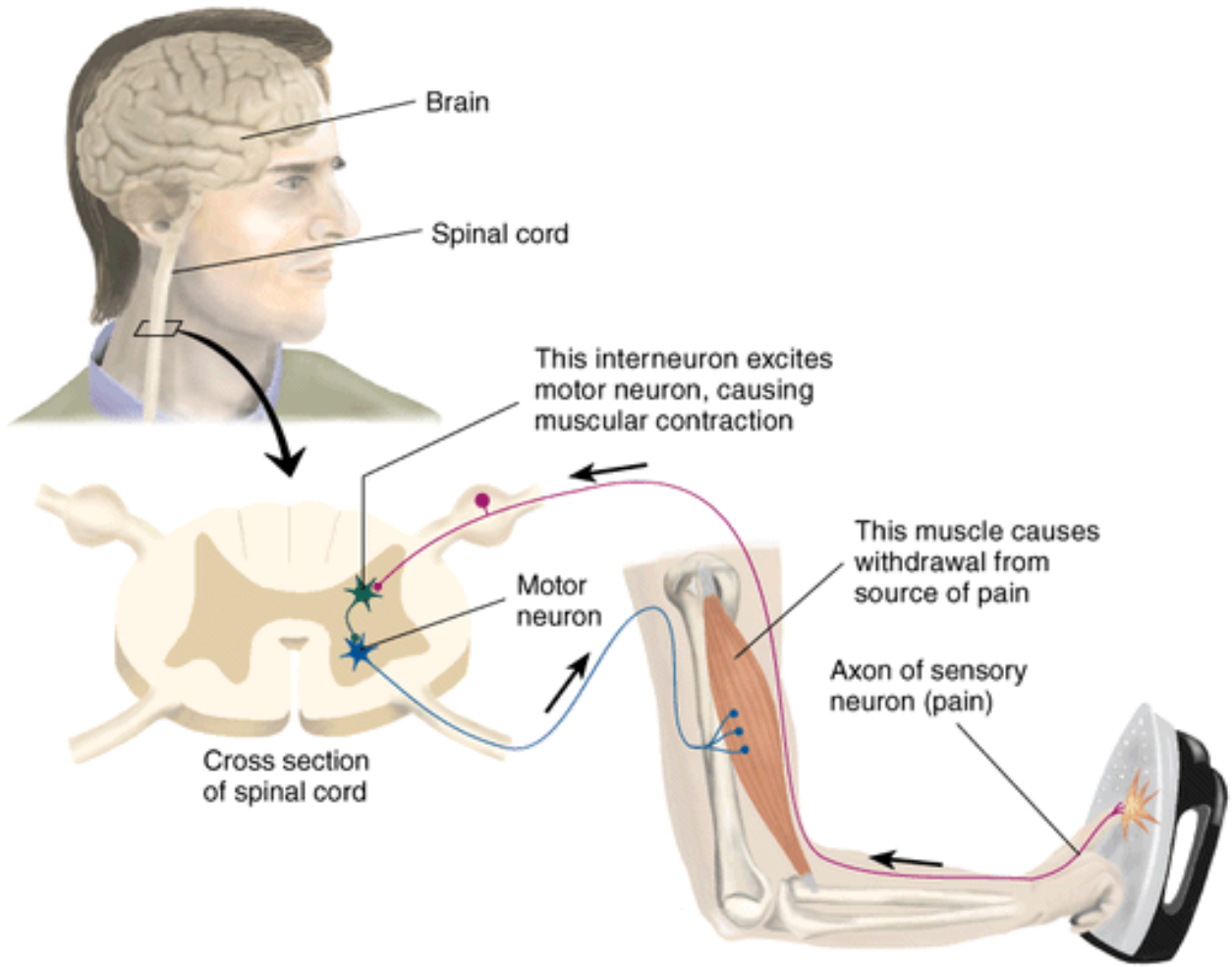
Peripheral Nervous System

Sub divided into

- Somatic nervous system
  - consist of sensory neurons that convey information from cutaneous and special sense receptors primarily in the head, body wall, and limbs to the CNS and
  - motor neurons from the CNS that conduct impulses to skeletal muscles only.
    - is voluntary



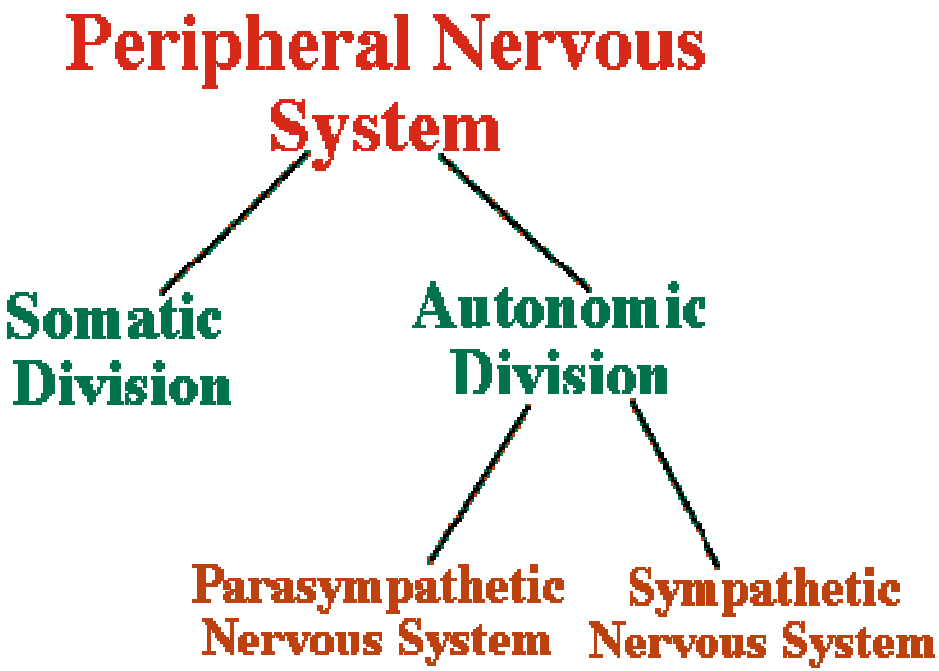
▶ A Withdrawal Reflex


Brain
Spinal cord
This interneuron excites motor neuron, causing muscular contraction
This muscle causes withdrawal from source of pain
Motor neuron
Axon of sensory neuron (pain)
Cross section of spinal cord

Peripheral Nervous System

- **Autonomic nervous system**
  - consist of motor neurons from the CNS that conduct impulses to smooth muscle, cardiac muscle, and glands.
  - Is involuntary

    Consist of two branches
    - **sympathetic**- controls those process that tend to expend energy (speedup heart beat).
    - **parasympathetic**- control those process that tend to conserve energy (slow the heart beat).



Nervous System Histology

Consist of two types of neurons

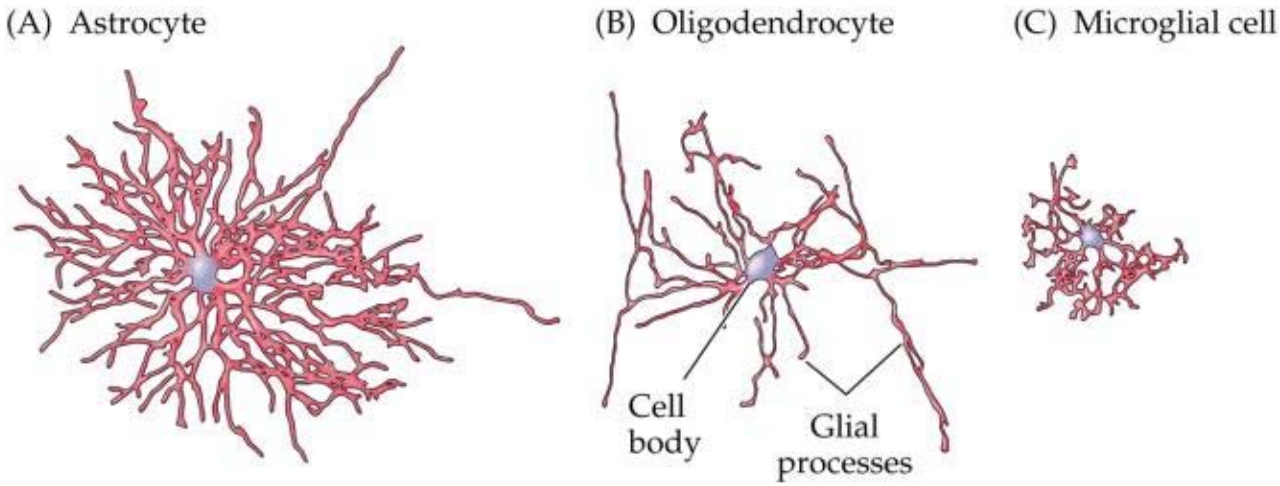
- **Neuroglia-** serve to support and protect the neurons.
  - generally smaller than neurons and outnumber neurons 5-50 times.
- **Neurons-** the main cell of the nervous system that is specialized for nerve impulse conduction.

<u>Neuroglia</u>

- Central Nervous System
  - Astrocytes
  - Oligodendrocytes
  - Microglia cells
  - Ependymal cells
- Peripheral neuroglia
  - schwann cells (neurolemmocytes)
  - satellite cells

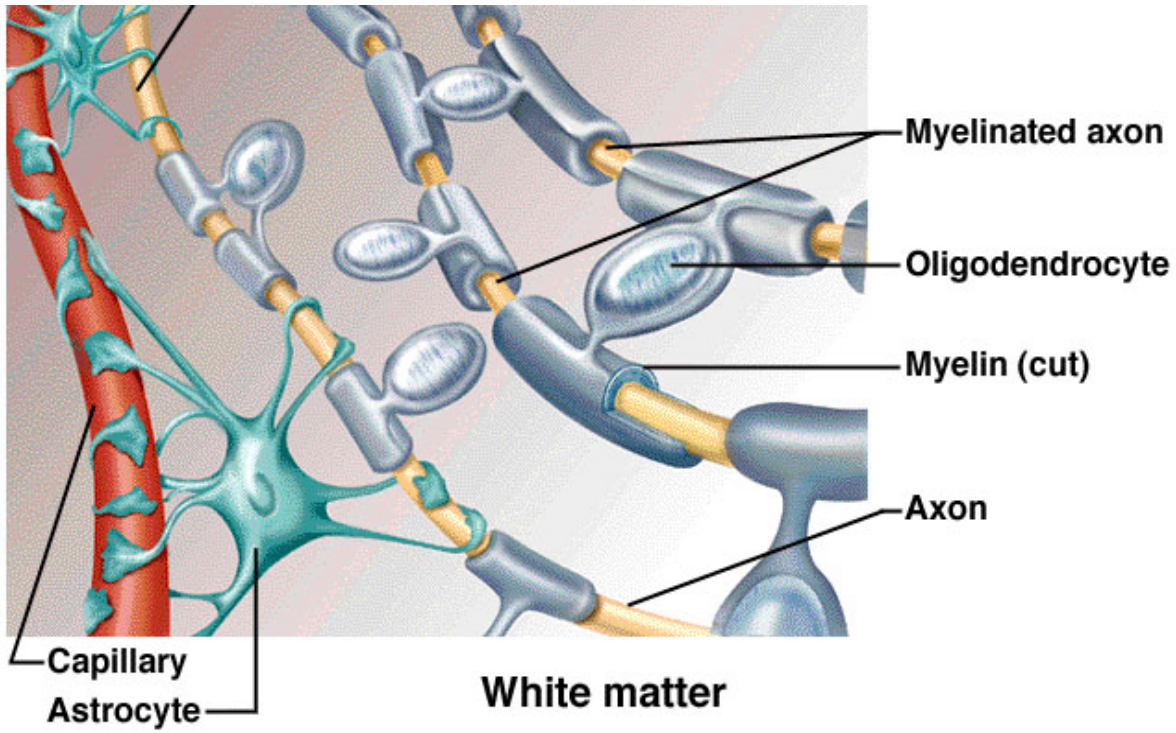
Central Nervous System Neuroglia

Glial cells in the CNS

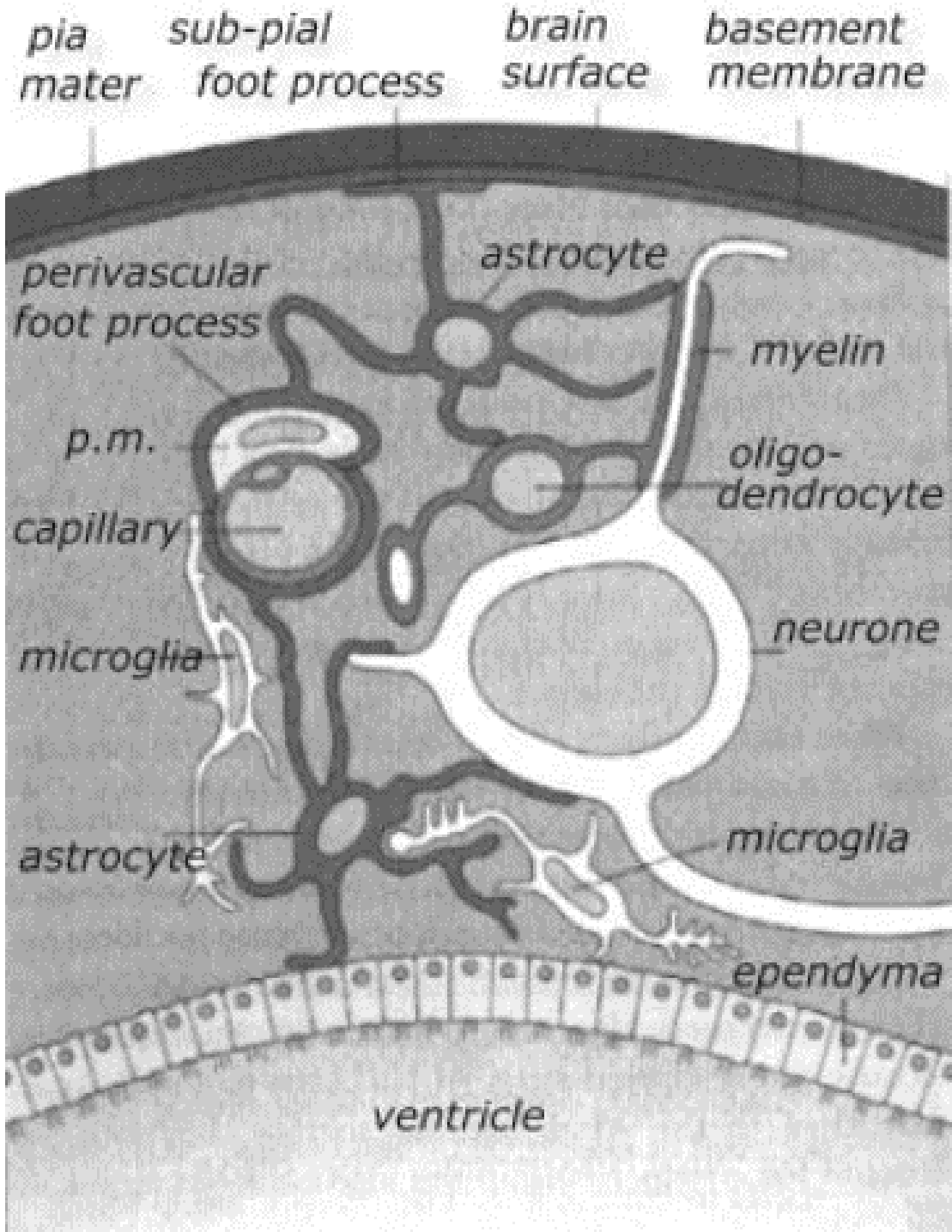


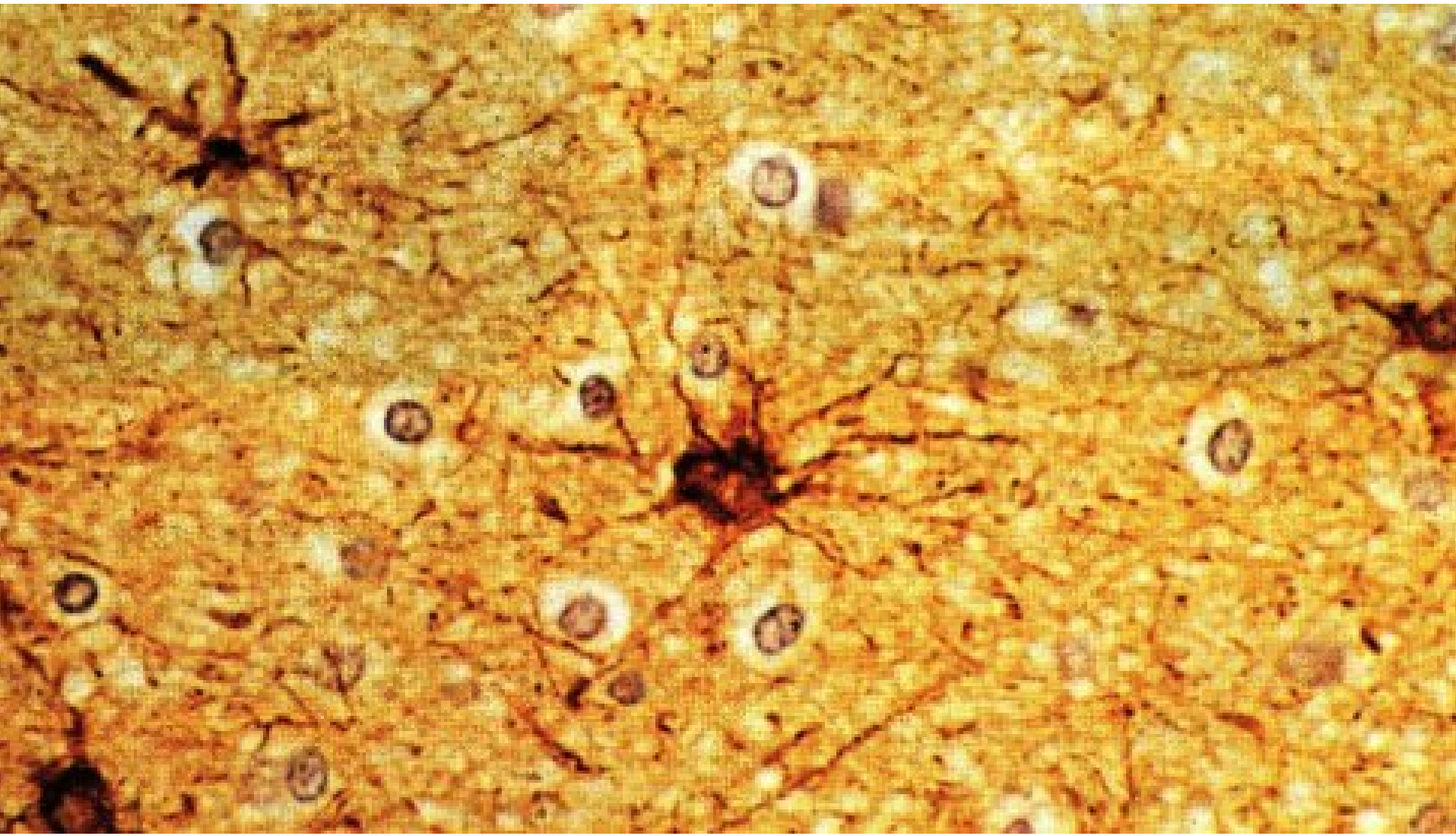
Central Nervous System Neuroglia

- **Astrocytes**
  - are the most abundant and functionally diverse
  - Help form the blood brain barrier with cytoplasmic extensions called perivasular feet that stimulate the endothelial cells to from tight junctions
  - convert glucose to lactate for neuronal nourishment
  - Participate in the metabolism of neurotransmitters
  - form brain scar tissue (**astrocytosis**, **gliosis** sclerosis)



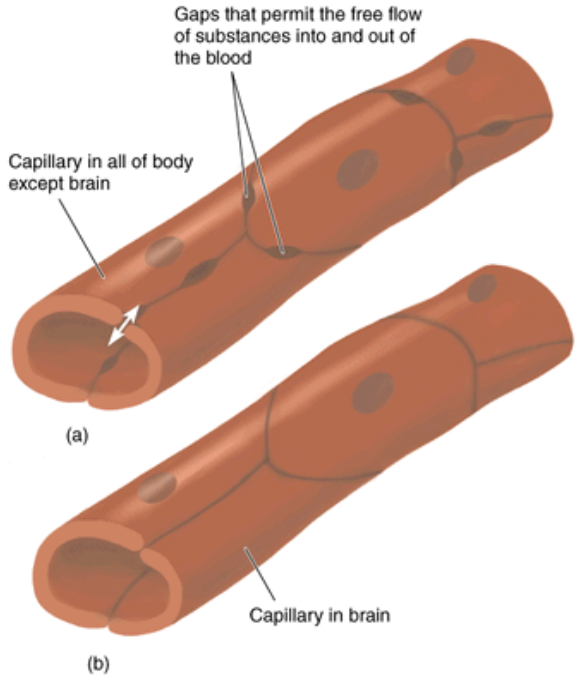
Astrocytes form end feet which form a barrier to materials passing into the CNS from the meninges. These end feet fuse with the innermost layer of the meninges called the pia mater and are called **sub-pial foot processes.**





Blood Brain Barrier

- Regulates the passage of substances into the brain
  - Capillary wall
  - Astrocyte processes


Gaps that permit the free flow of substances into and out of the blood
Capillary in all of body except brain
(a)
Capillary in brain
(b)

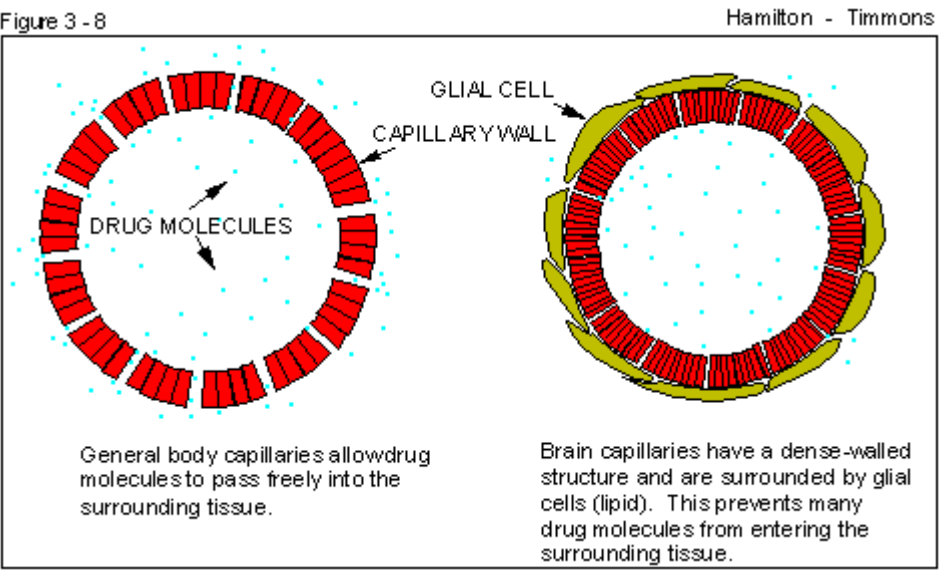
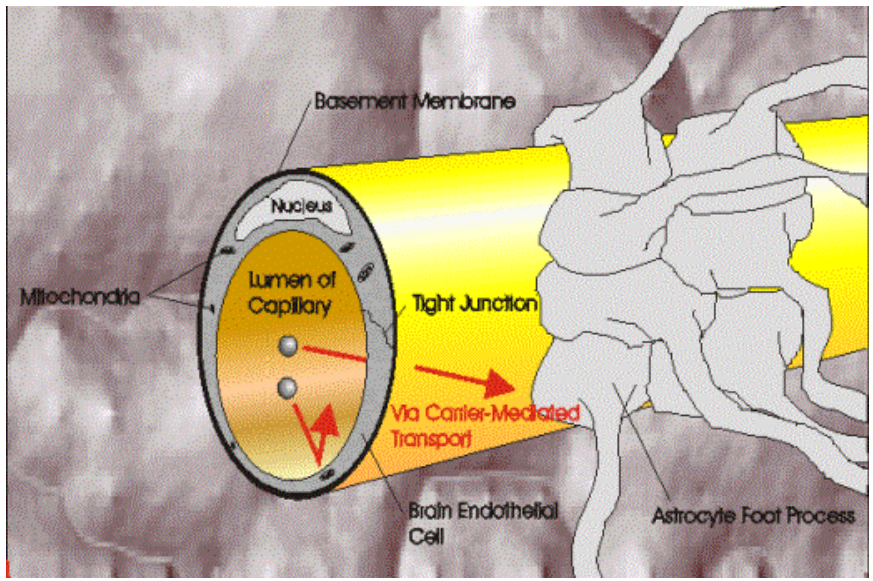
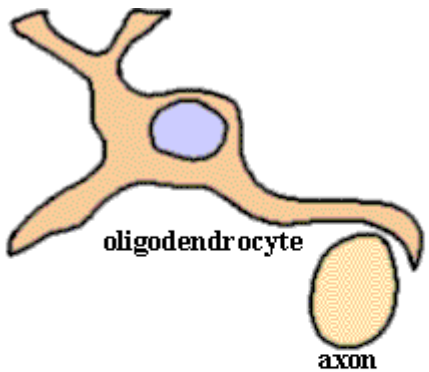


Figure 3 - 8
Hamilton - Timmons
GLIAL CELL
CAPILLARY WALL
DRUG MOLECULES
General body capillaries allowdrug molecules to pass freely into the surrounding tissue.
Brain capillaries have a dense-walled structure and are surrounded by glial cells (lipid). This prevents many drug molecules from entering the surrounding tissue.



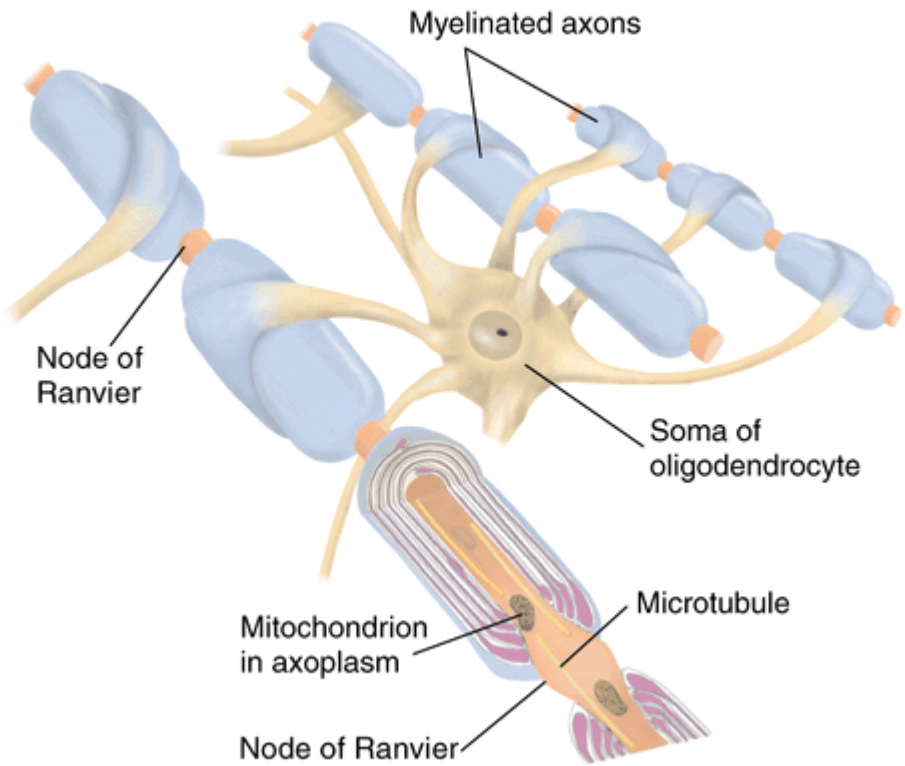
Central Nervous System Neuroglia

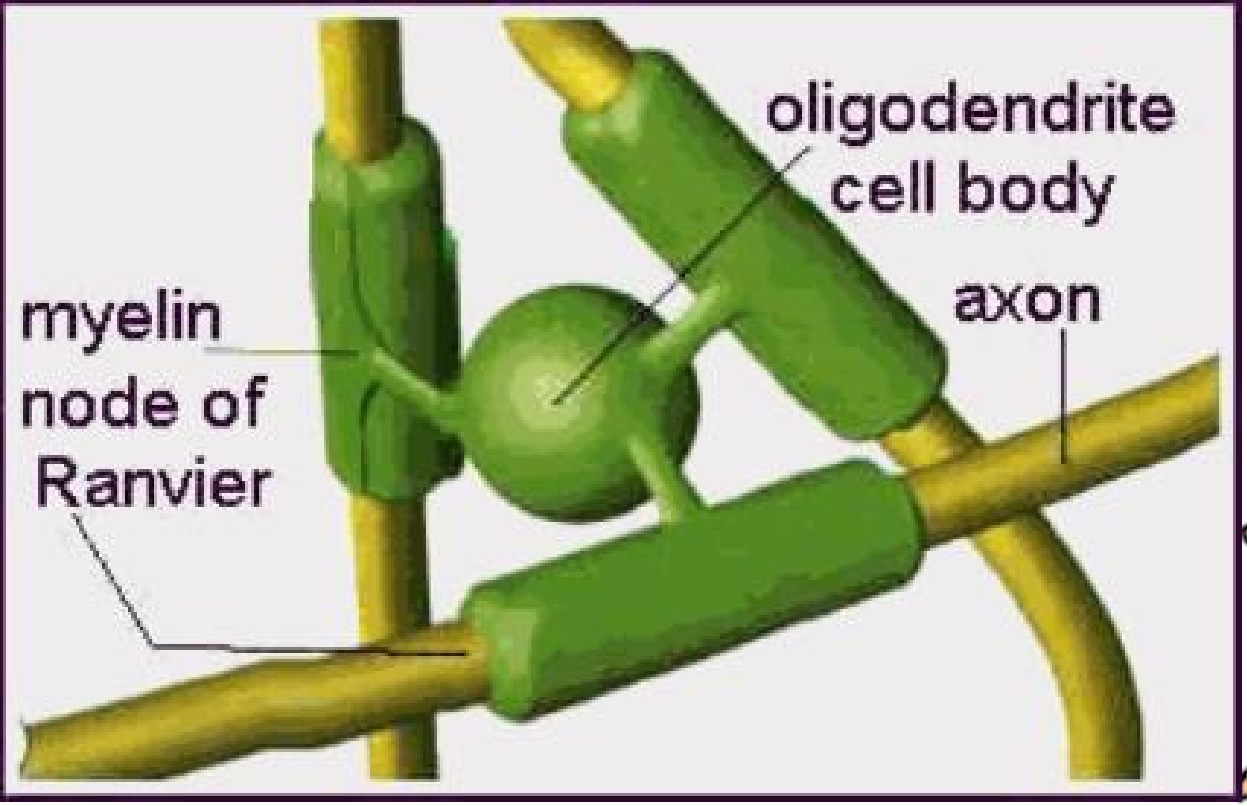
- Oligodendrocyte
  - Form myelin sheath around CNS neurons

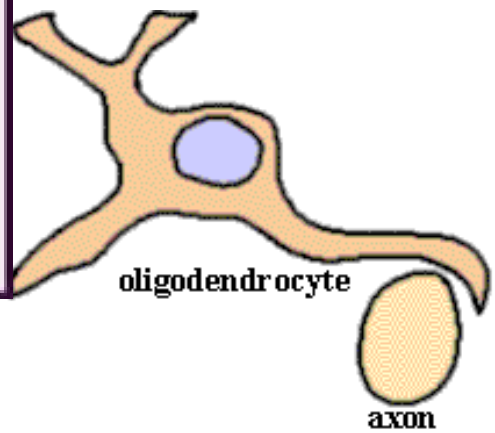


The Process of Myelination

► An Oligodendrocyte







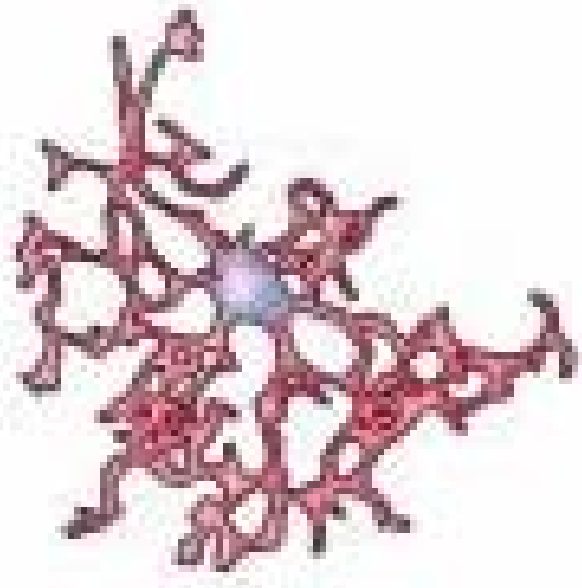
The Process of Myelination

Oligodendrocytes forms myelin in the CNS.

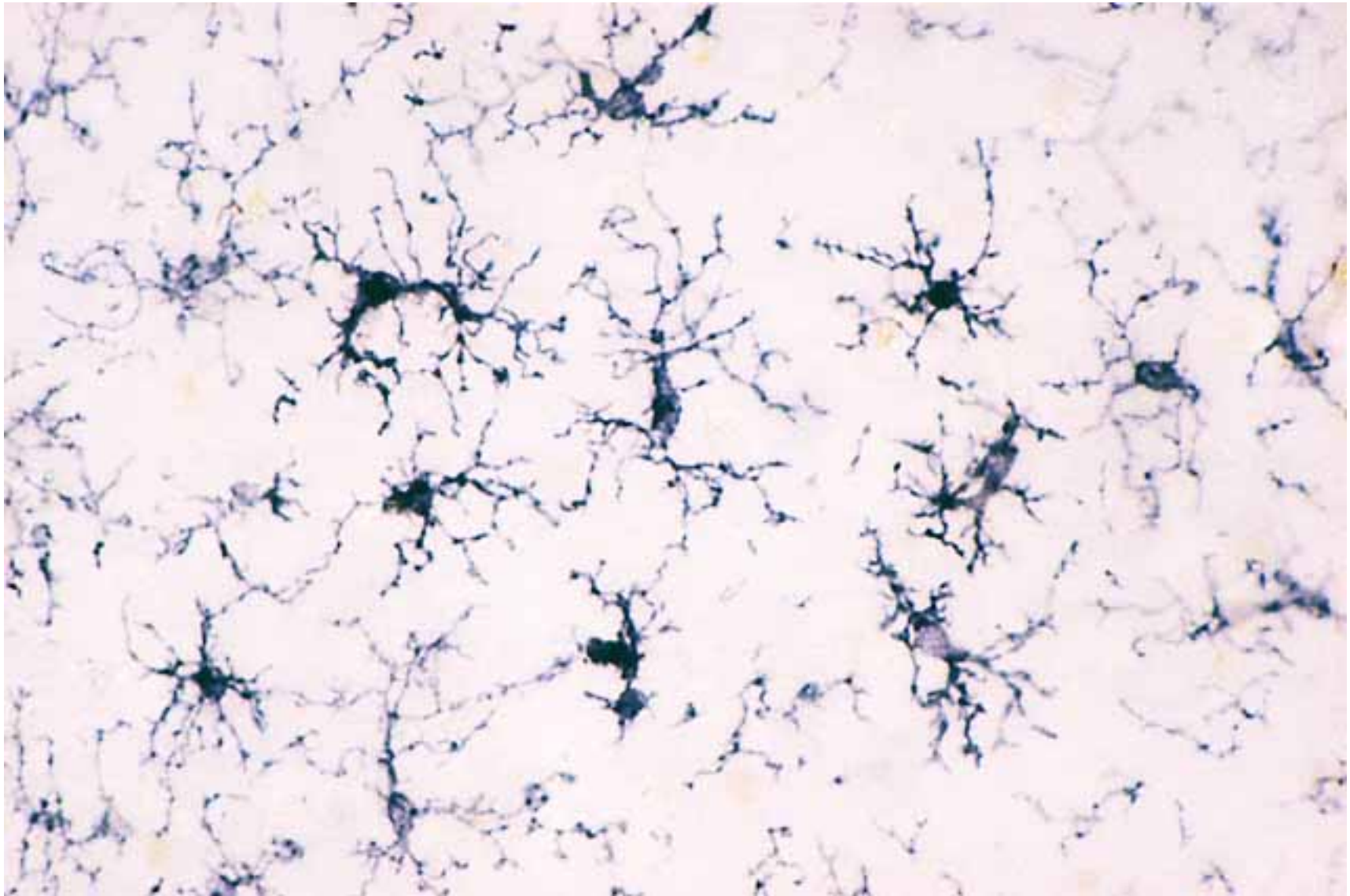
- Myelin is deposited with no neurolemma formed.
- Axons in the CNS display little regrowth after injury which is thought to be partly because of the lack of a neurolemma.

Central Nervous System Neuroglia

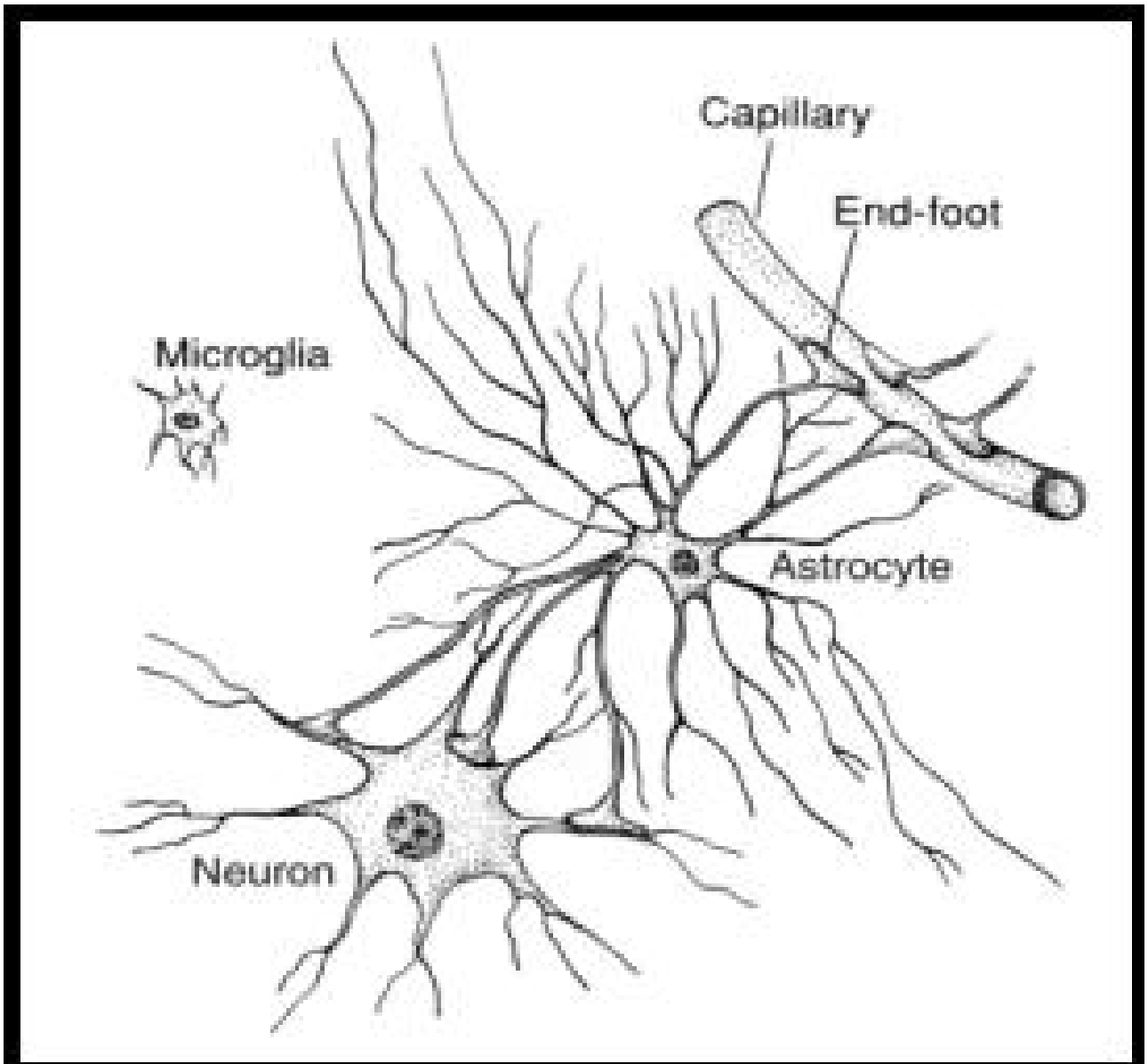
- Microglia
  - Phagocytic cells that engulf destroy microbes and cellular debris in the CNS
  - active in response to inflammation or injury



Microglia

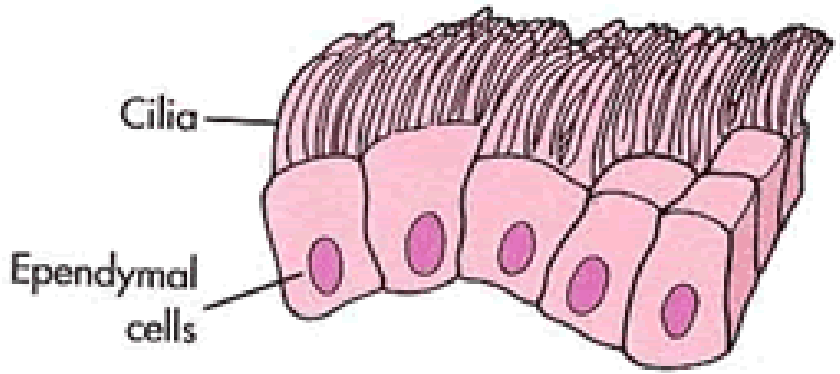


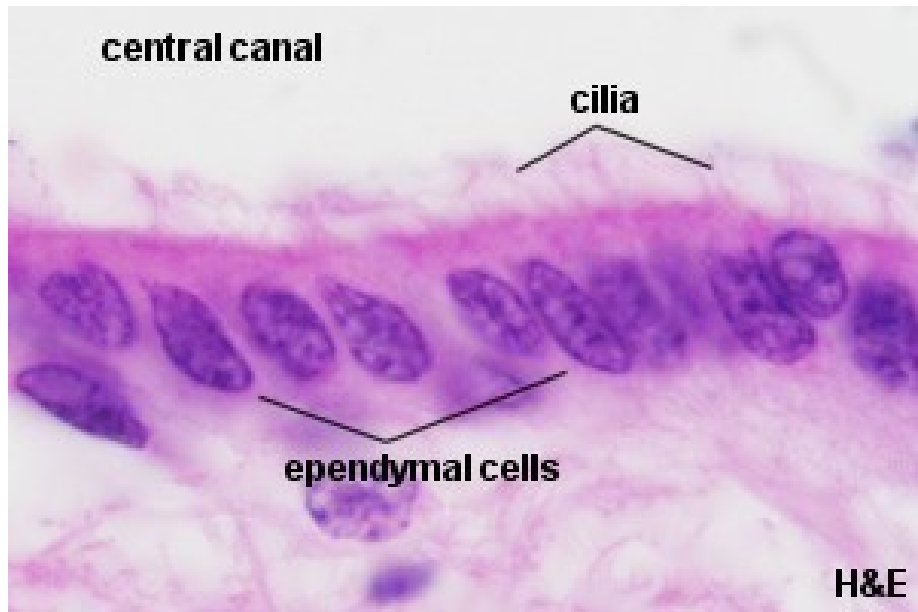
Astrocyte & Microglia



Central Nervous System Neuroglia

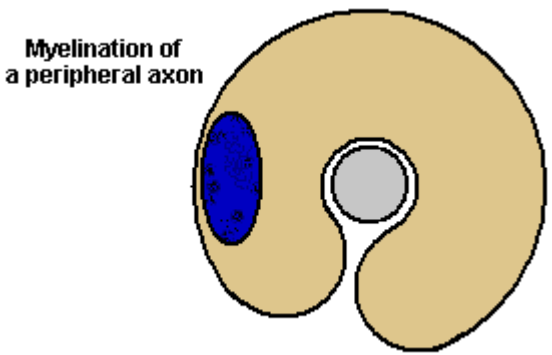
- Ependymal Cells-
  - Line the ventricles (spaces filled with CSF) of the brain and the central canal of the spinal cord
  - Produce cerebrospinal fluid
  - Assist in the circulation of the CSF

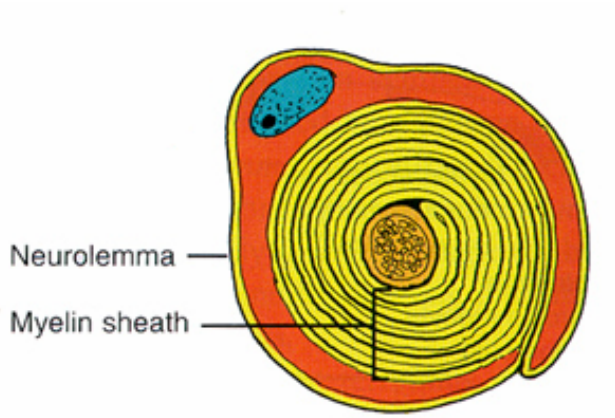


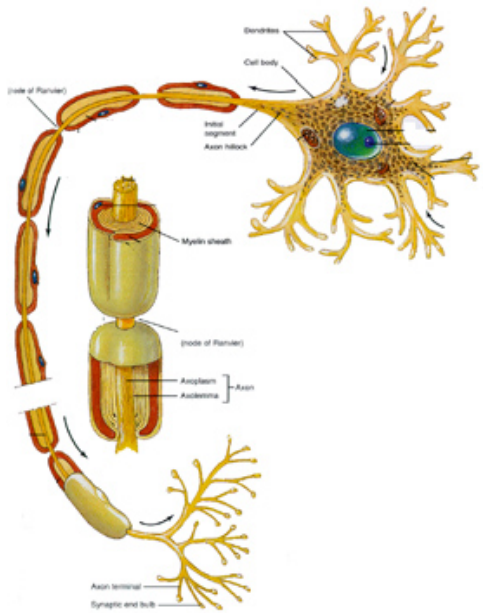


Peripheral Nervous System Neuroglia

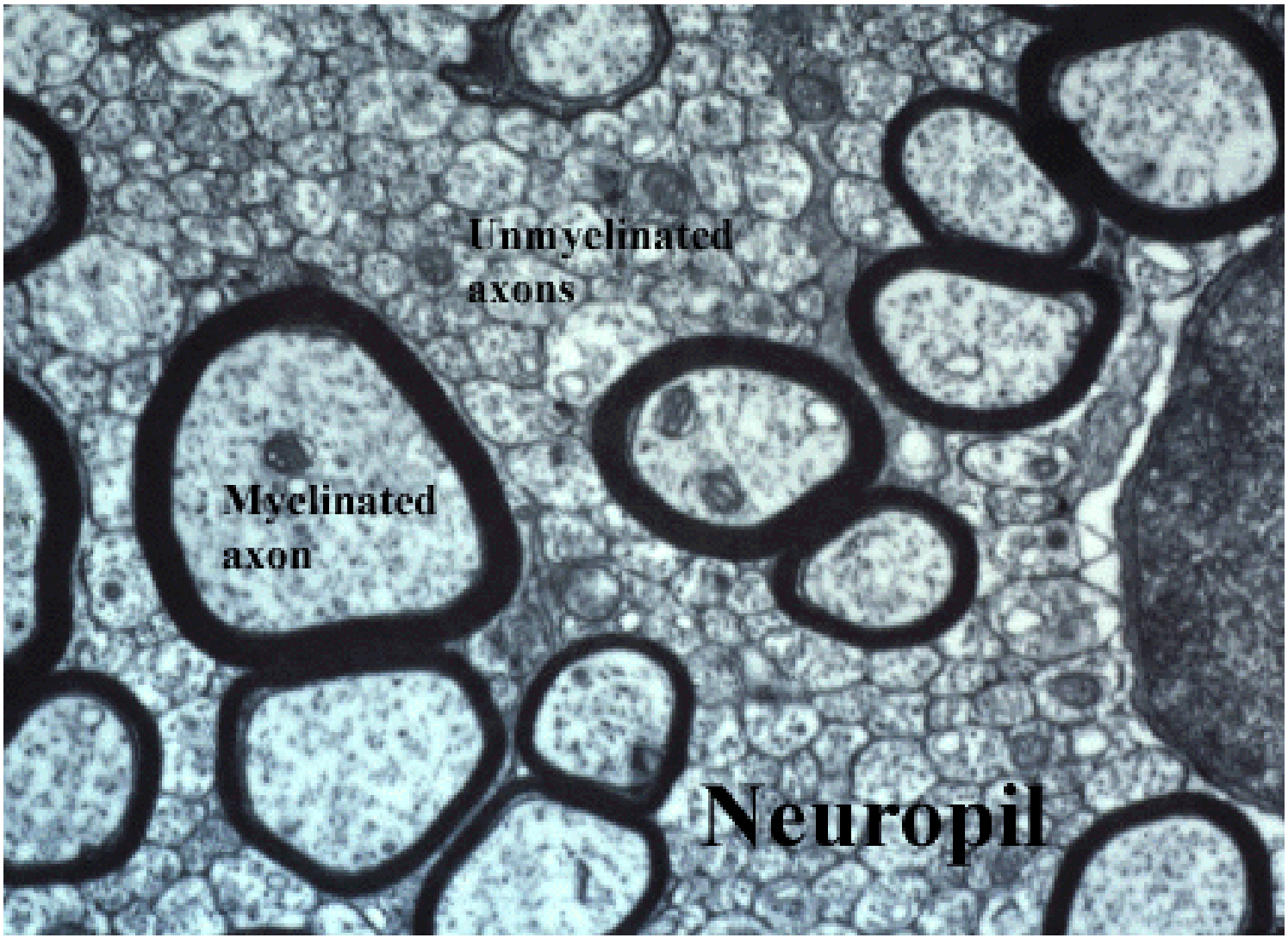
- **Schwann cells** (neurolemmocytes) Each cells produces part of the myelin sheath around a single axon in the PNS.
  - **Neurolemma** (sheath of Schwann)- the outer nucleated cyotplasmic layer of the neurolemmocyte.
  - **Nodes of Ranvier** (neurofibral nodes)- periodic gaps in the myelin sheath.





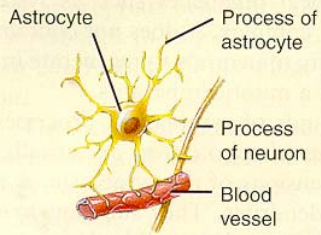
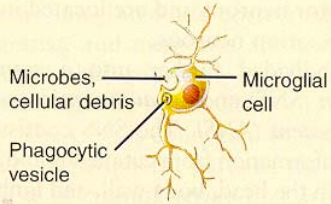
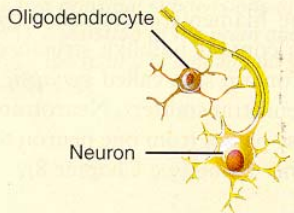
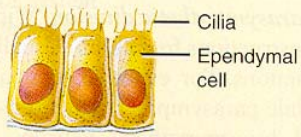
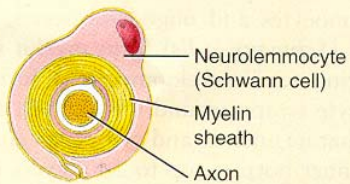
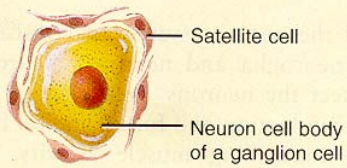


Myelinated Axons



Satellite Cells

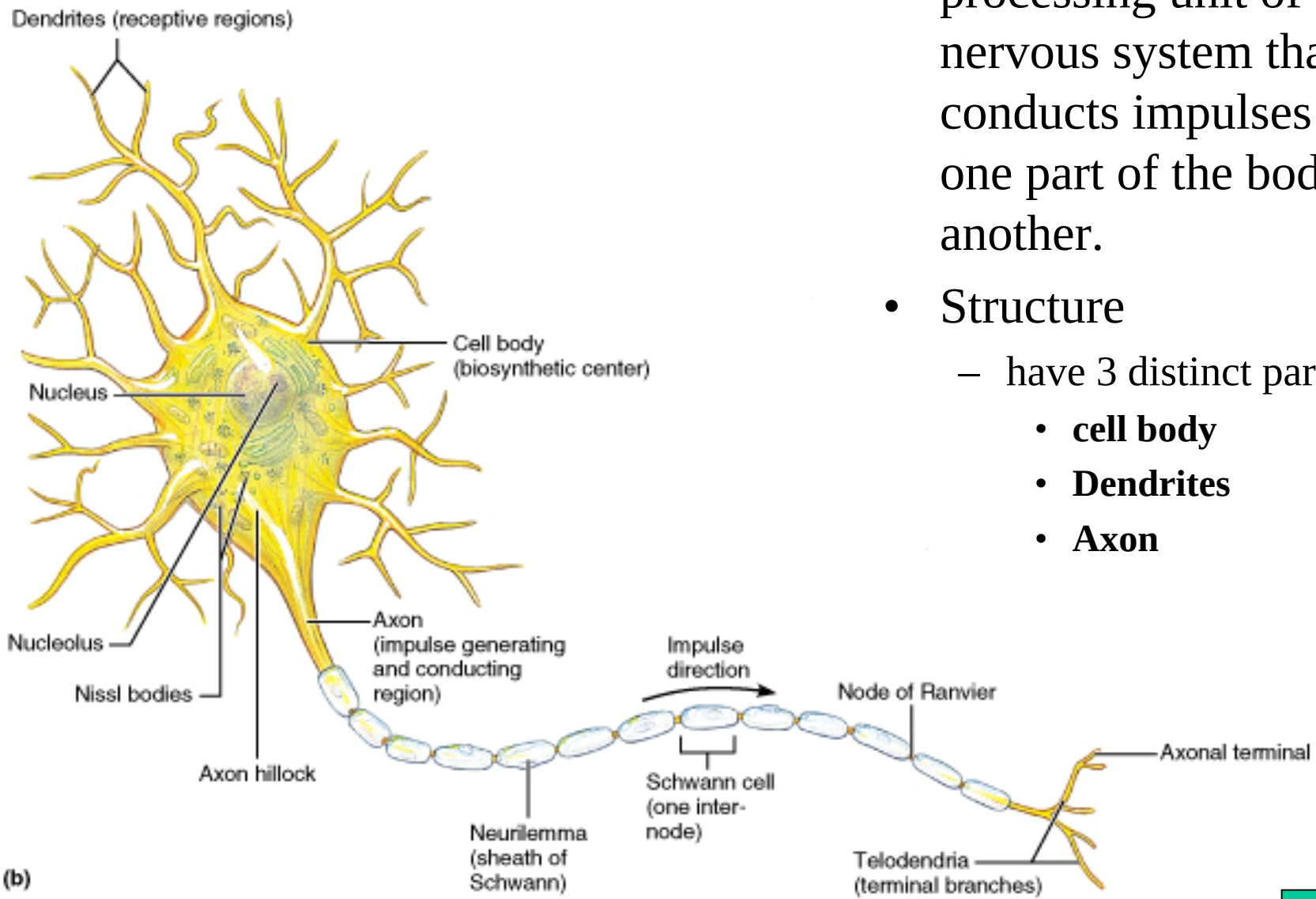
- surround the neuron cell bodies in ganglia of the PNS. Little is known of their function.

TYPE, MICROSCOPIC APPEARANCE AND DESCRIPTION	FUNCTIONS	TYPE, MICROSCOPIC APPEARANCE, AND DESCRIPTION	FUNCTIONS
CENTRAL NERVOUS SYSTEM NEUROLOGIA			
Astrocytes (AS-trō-sīts; *astro* = star; *cyte* = cell)  Star-shaped cells with many processes.	Participate in the metabolism of neurotransmitters and maintain the proper balance of K^+ for generation of nerve impulses by CNS neurons; participate in brain development; help form the blood–brain barrier that regulates the passage of substances into the brain.	**Microglia** (mī-KROG-lē-a; *micro* = small; *glia* = glue)  Small cells with few processes.	Phagocytic cells that engulf and destroy microbes and cellular debris in the CNS.
Oligodendrocytes (OL-i-gō-den′-drō-sīts; *oligo* = few; *dendro* = tree)  Smaller than astrocytes with fewer processes; round or oval cell body.	Produce myelin sheath around axons of neurons of CNS; each oligodendrocyte wraps myelin around several axons.	**Ependymal** (ep-EN-di-mal; *ependyma* = upper garment) **cells**  Epithelial cells arranged in a single layer; many are ciliated.	Line the ventricles of the brain (spaces filled with cerebrospinal fluid) and the central canal of the spinal cord; form cerebrospinal fluid (CSF) and assist in the circulation of CSF.
PERIPHERAL NERVOUS SYSTEM NEUROLOGIA			
Neurolemmocytes (noo′-rō-LE-mō-sīts) or **Schwann cells**  Flattened cells arranged around axons in PNS.	Each cell produces part of the myelin sheath around a single axon of a PNS neuron.	**Satellite** (SAT-i-līt) **cells**  Flattened cells arranged around the cell bodies of neurons in ganglia (collections of neuronal cell bodies in the PNS).	Support neurons in ganglia of PNS.

Neuron

The basic information processing unit of the nervous system that conducts impulses from one part of the body to another.

- Structure
  - have 3 distinct parts
    - **cell body**
    - **Dendrites**
    - **Axon**



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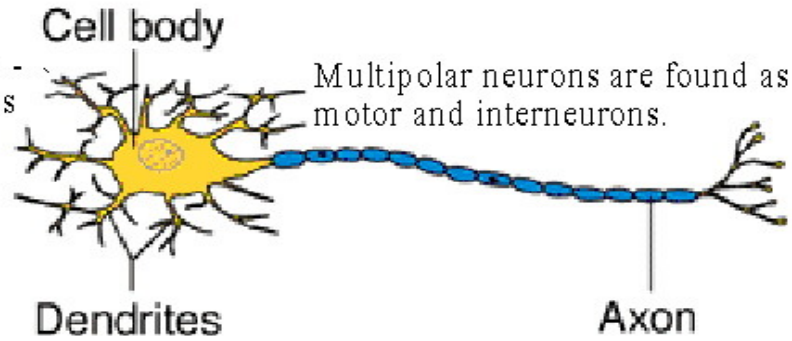
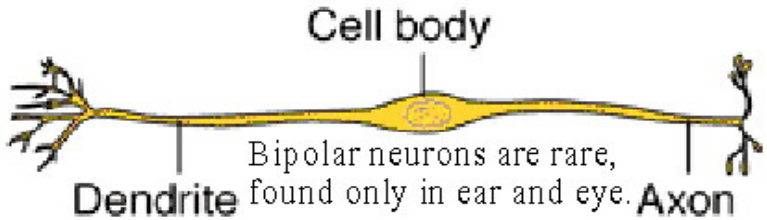
Structural Classes of Neurons

Multipolar neuron - has many dendrites and one axon.



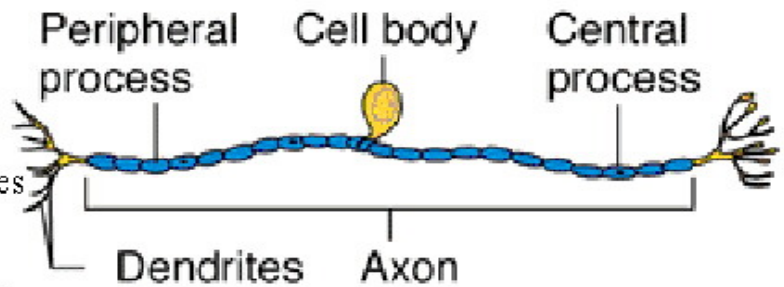
Multipolar neurons are found as motor and interneurons.

Bipolar neuron - has one dendrite and one axon attached to the cell body.



Bipolar neurons are rare, found only in ear and eye.

Unipolar neurons have one process from the cell body, an axon. It branches to connect to receptors and the spinal cord or brain.

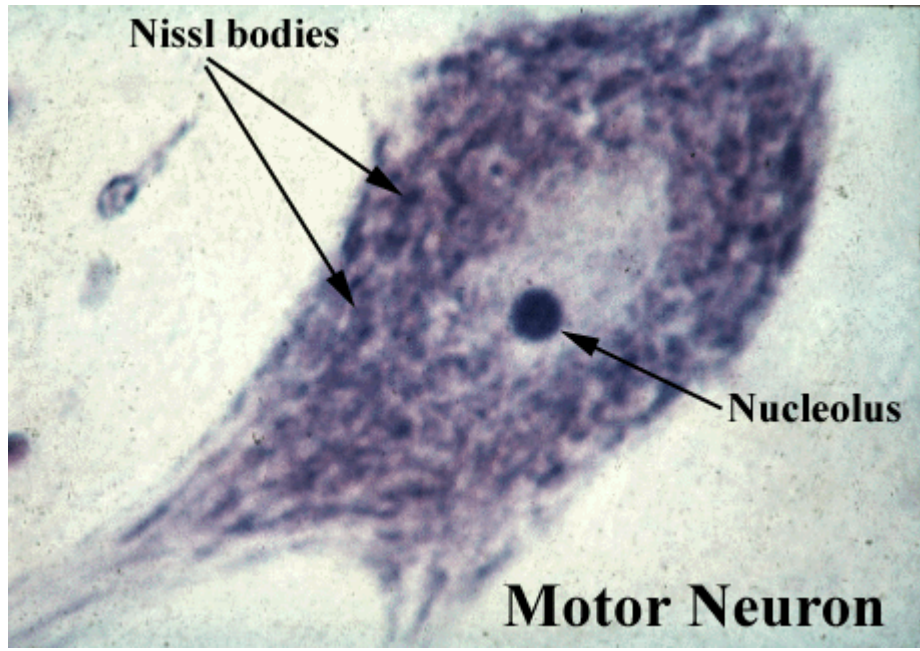


Unipolar neurons are most of the body's sensory neurons. The dendrites are found at the receptor and the axon leads to the spinal cord or brain.

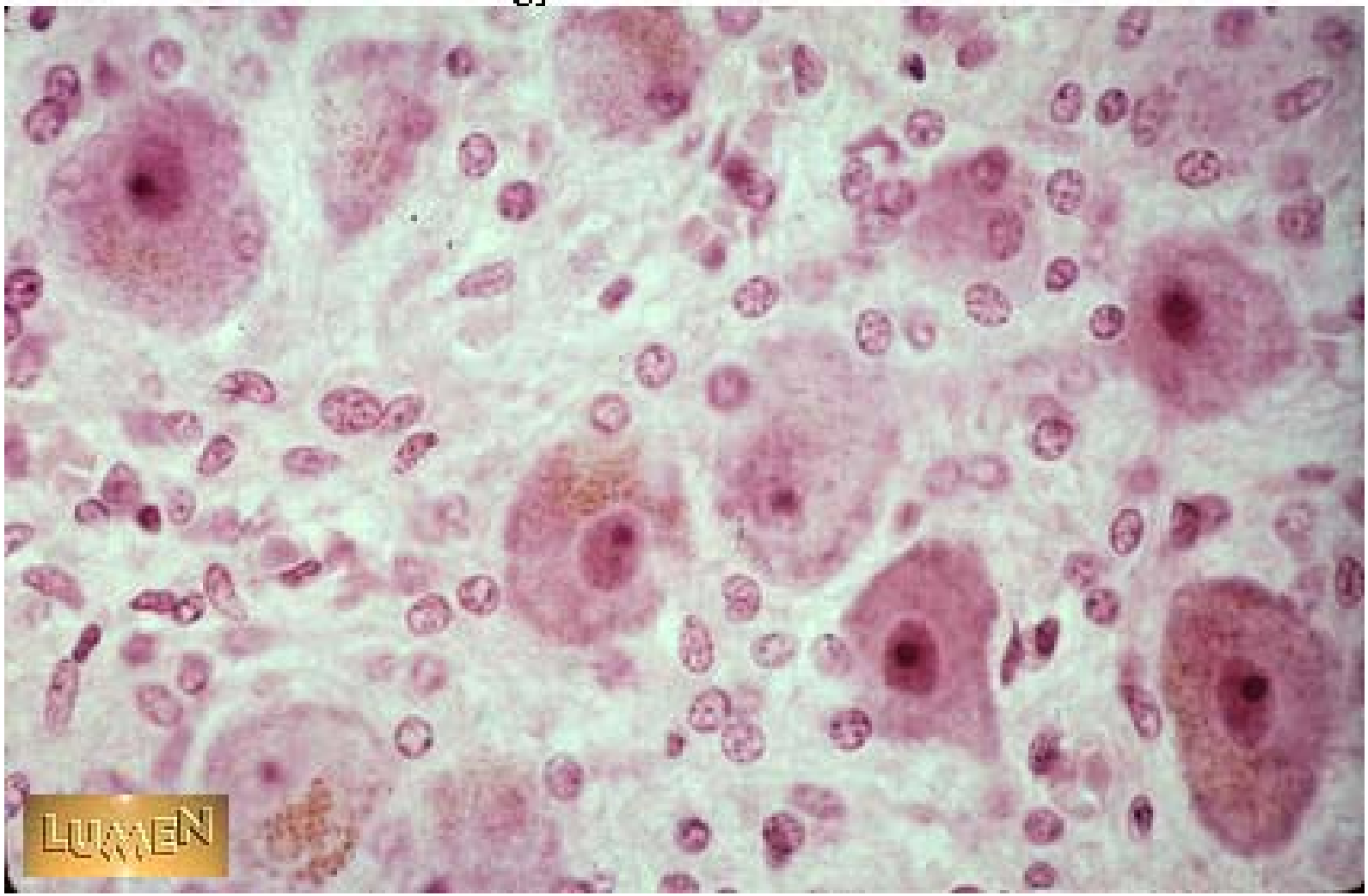
Neuron Cell Body

(soma, perikaryon)-
contains a nucleus with a prominent nucleous surrounded by a granular cytoplasm and various organelles.

- •does not contain a mitotic apparatus as a result, neurons do not divide
- •has distinctive cytoplasmic feature called **Nissl bodies-** rough ER formed into large bodies seen in the light microscope as dark staini granules



Histology Lab Part 6: Slide 10



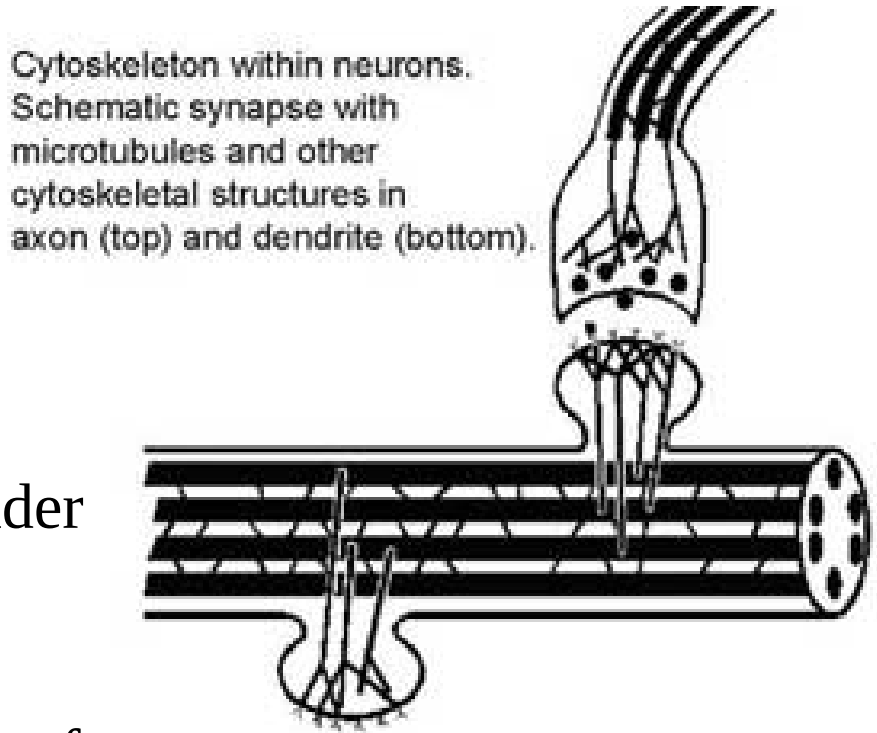
Lipfuscin- golden brown pigmented cytoplasmic inclusion

- an end product of lysosomal digestion of worn-out organelles and other products (wear and tear granules)
- collects with age and pushes the nucleus aside
- abundant in all neurons and re harmless

Cytoskeleton

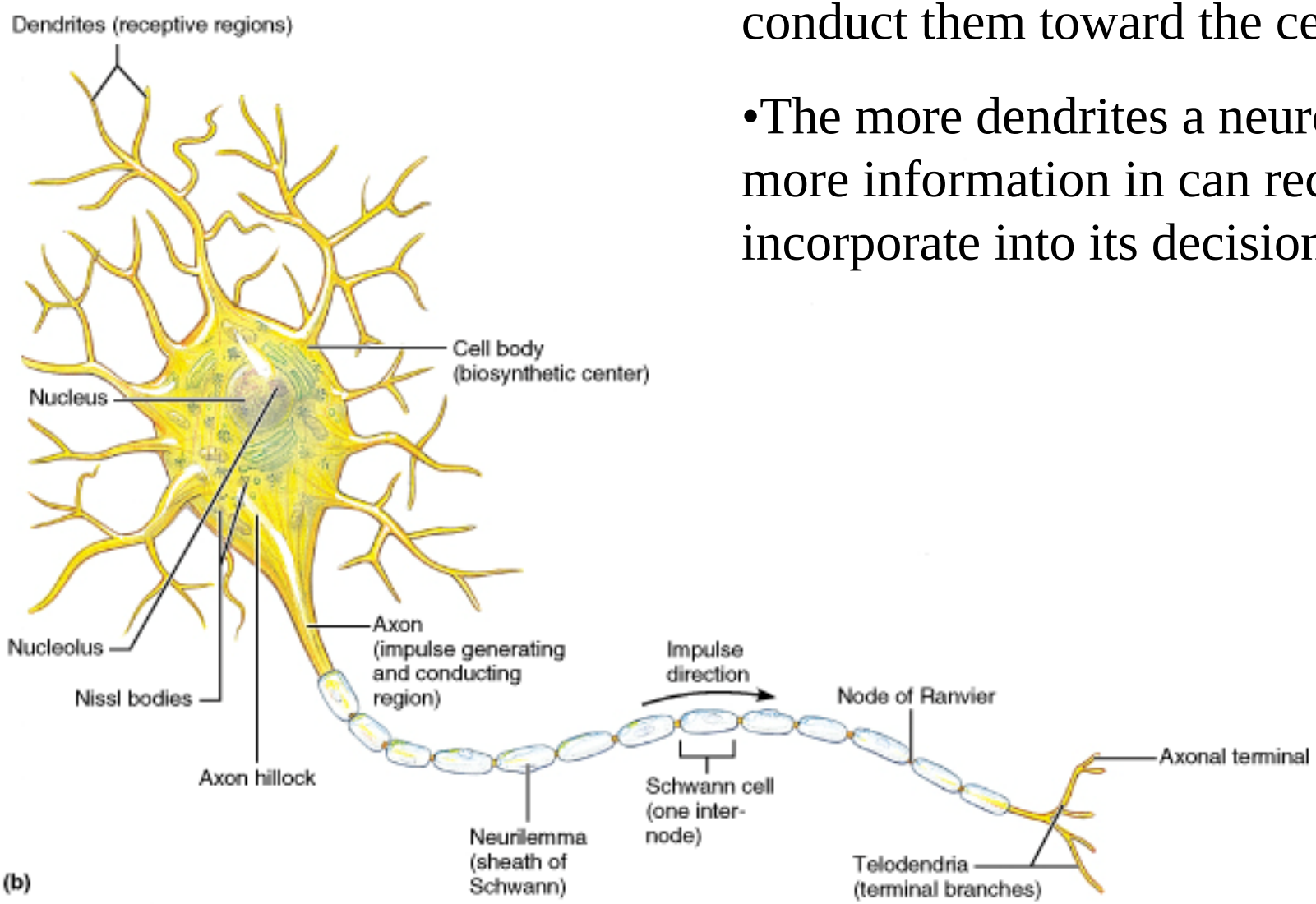
Has an extensive network of microtubles, microfilaments,and neurofilaments

- **Microtubles-** tracks along which organelles are transported
- **Microfilaments-**actin, located under plasma membrane, contractile, transport materials down axon
- **Neurofilaments-** maintains shape of cell, main support for cell, **neurofibrils** (bundles of neurofilaments



Dendrites- short, thick, highly branched cytoplasmic process that functions to receive impulses and conduct them toward the cell body.

•The more dendrites a neuron has, the more information in can receive and incorporate into its decision making.



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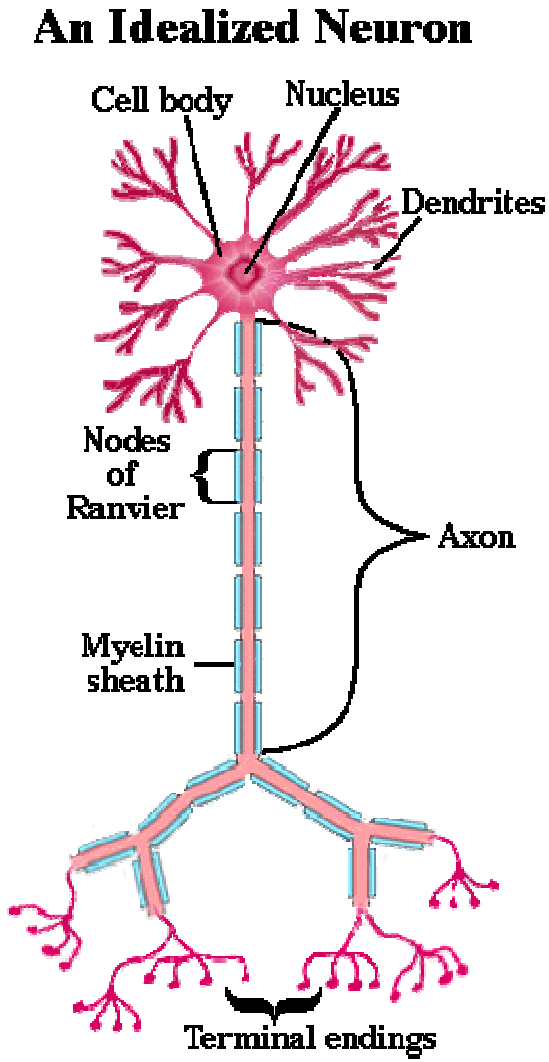
Axon- a single long, thin extension that sends impulses to another neuron or tissue.

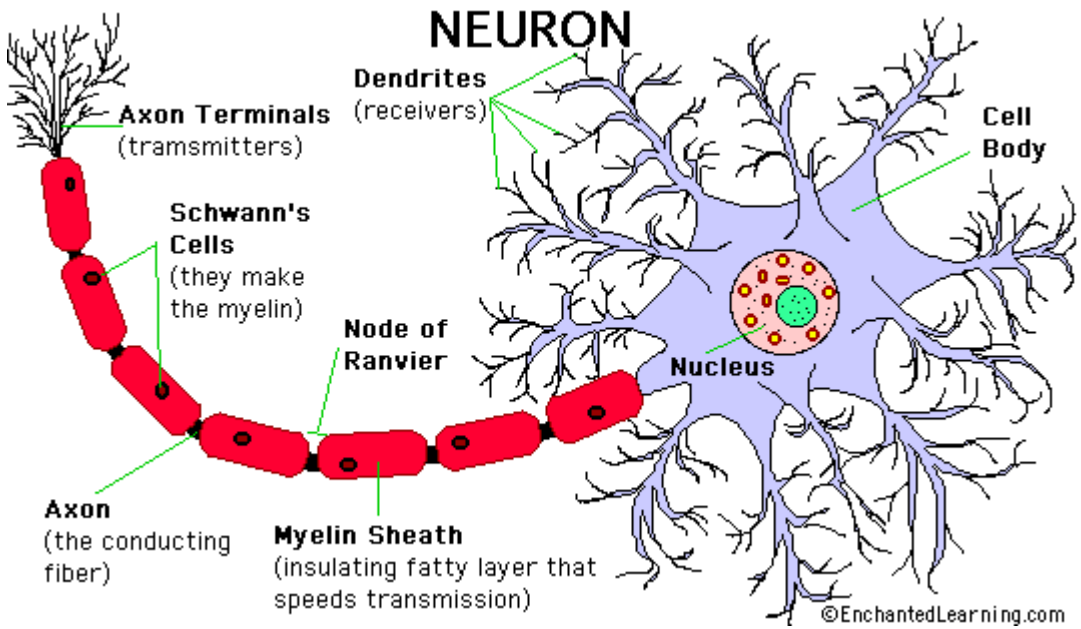
- **Axon hillock-** where axon originates (does not contain Nissl bodies)
- Vary in length from .04 inches to 3.28 feet
- **axon collaterals-** side branches along the length of the axon
- **axon terminals-** many tiny end filaments derived from branching of axon and collaterals
- **synaptic bulbs (knob)-** bulb-like structures at the end of axon terminals which contain synaptic vesicles that store neurotransmitters.

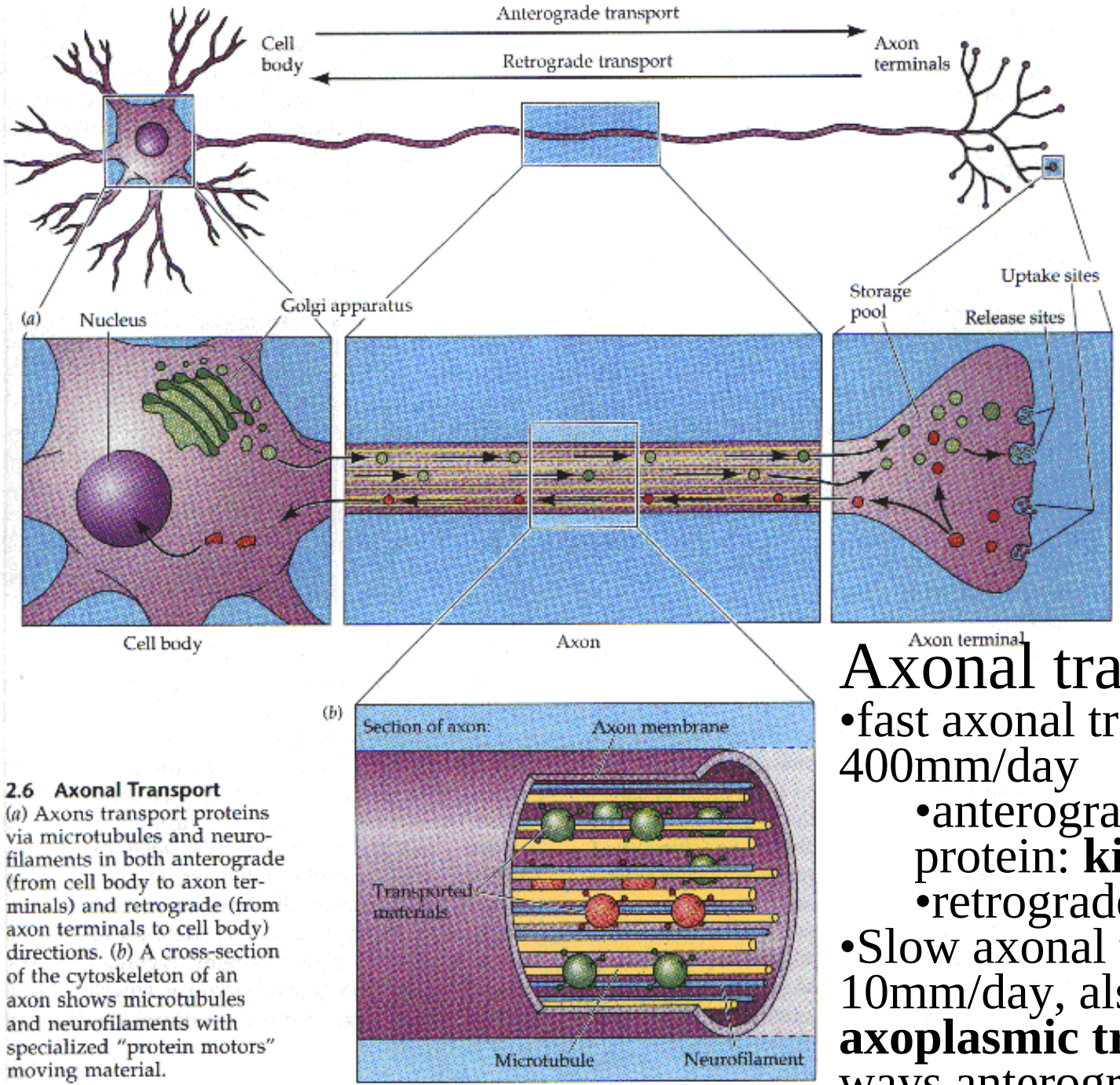
•cytoplasm called **axoplasm**

•limiting membrane called **axolemma**



Most axons are surrounded by a many layered white, lipid and protein covering produced by neuroglia called **myelin sheath**.
It electrically insulates the axon and increases the speed of nerve impulse conduction.
Axons with myelin sheaths are said to be myelinated and those without are unmyelinated.

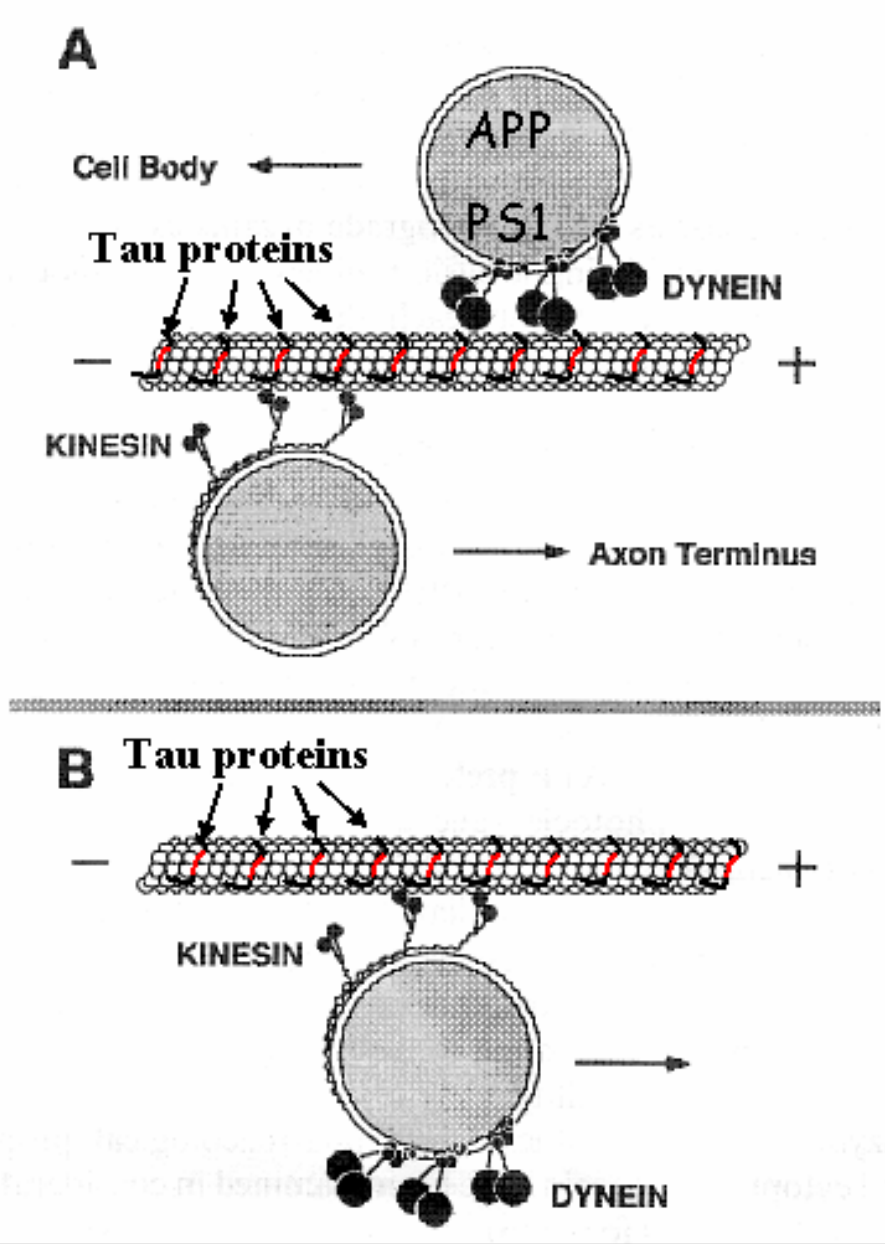




2.6 Axonal Transport
(*a*) Axons transport proteins via microtubules and neurofilaments in both anterograde (from cell body to axon terminals) and retrograde (from axon terminals to cell body) directions. (*b*) A cross-section of the cytoskeleton of an axon shows microtubules and neurofilaments with specialized "protein motors" moving material.

Axonal transport

- fast axonal transport, 400mm/day
  - anterograde- motor protein: **kinesin**
  - retrograde- **dynein**
- Slow axonal transport, 10mm/day, also called **axoplasmic transport** all ways anterograde



Axonal transport

• Fast axonal transport, 400mm/day

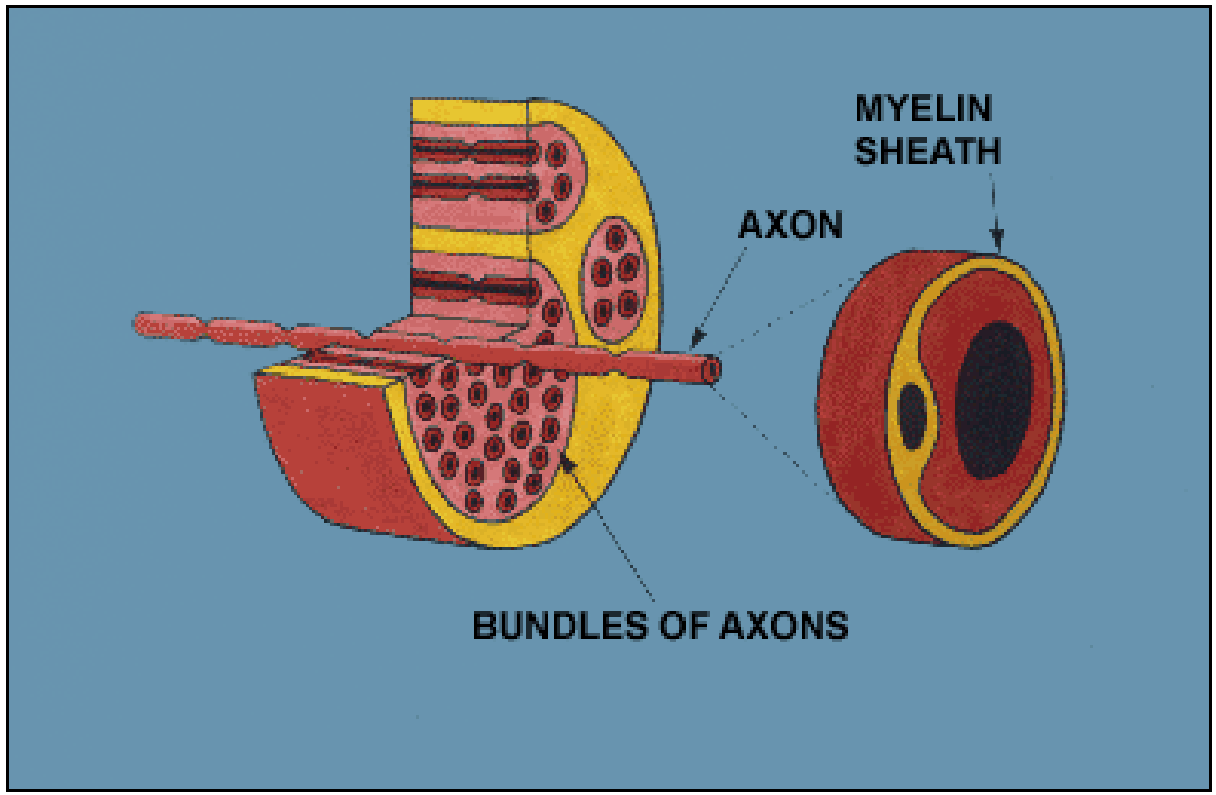
-anterograde- motor protein: **kinesin**

-retrograde- **dynein**

•Slow axonal transport, 10mm/day, also called **axoplasmic transport** all ways anterograde

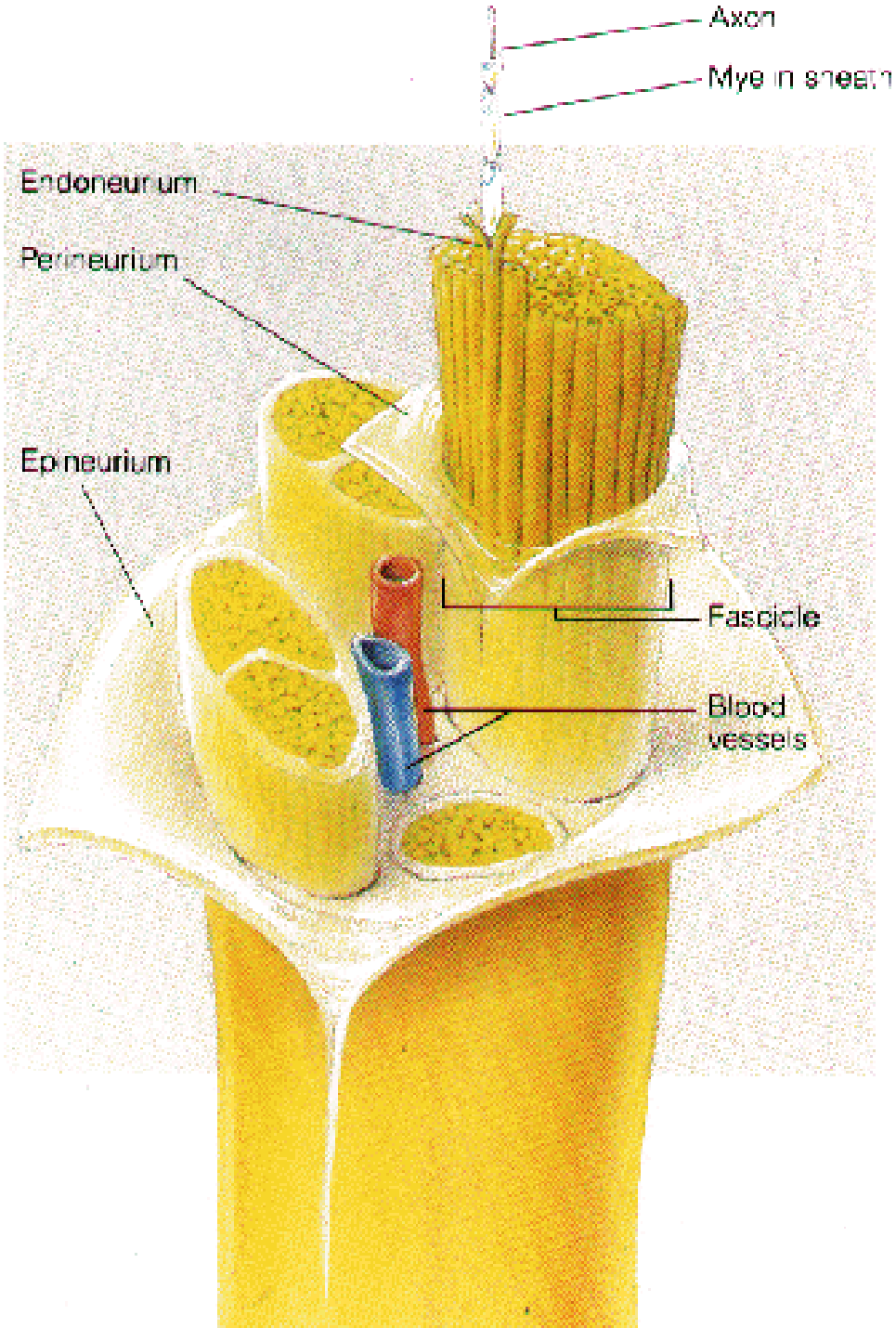
•motor proteins carry materials “on their backs” while they reach out, like myosin heads of muscle, to bind repeatedly to the microtubules and crawl along them.

Grouping of Neural Tissue



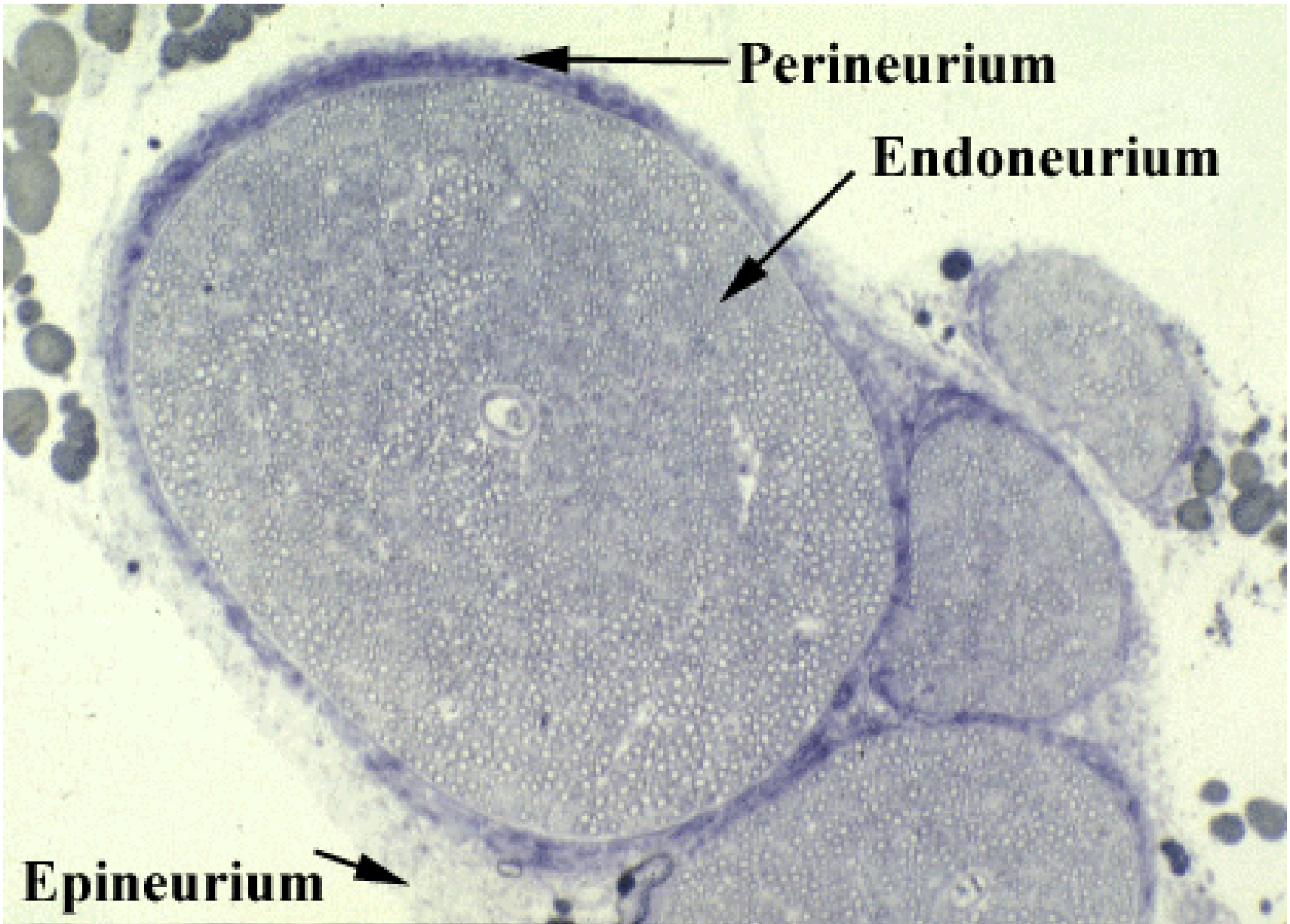
Nerve fiber- any process projecting from the cell body (dendrite or axon).

Nerve- a group of myelinated nerve fibers in the PNS.
most nerves contain both sensory and motor fibers


Axon
Myelin sheath
Endoneurium
Perineurium
Epineurium
Fascicle
Blood vessels

Peripheral Nerve

Peripheral Nerve



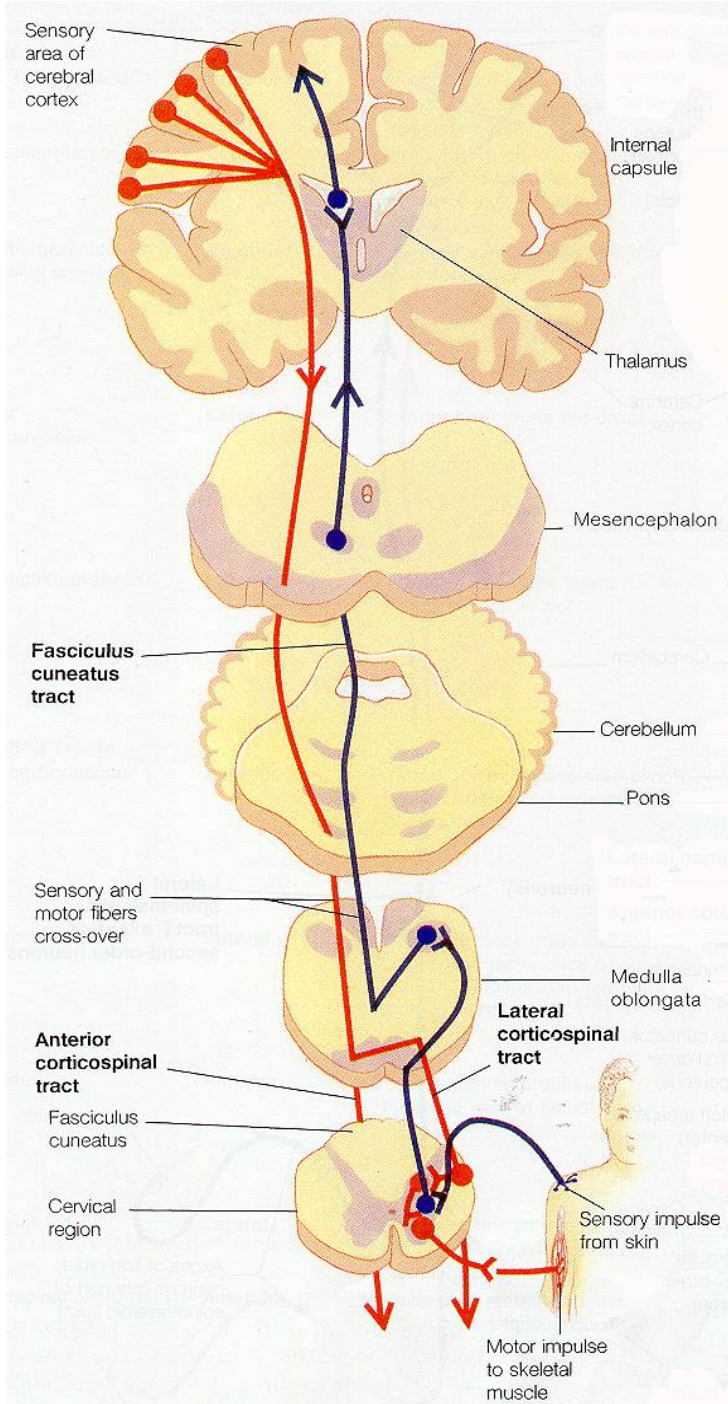
Grouping of Neural Tissue

White matter- a group of myelinated axons from many cell bodies

Tract- indicates a bundle of fibers located in the CNS.

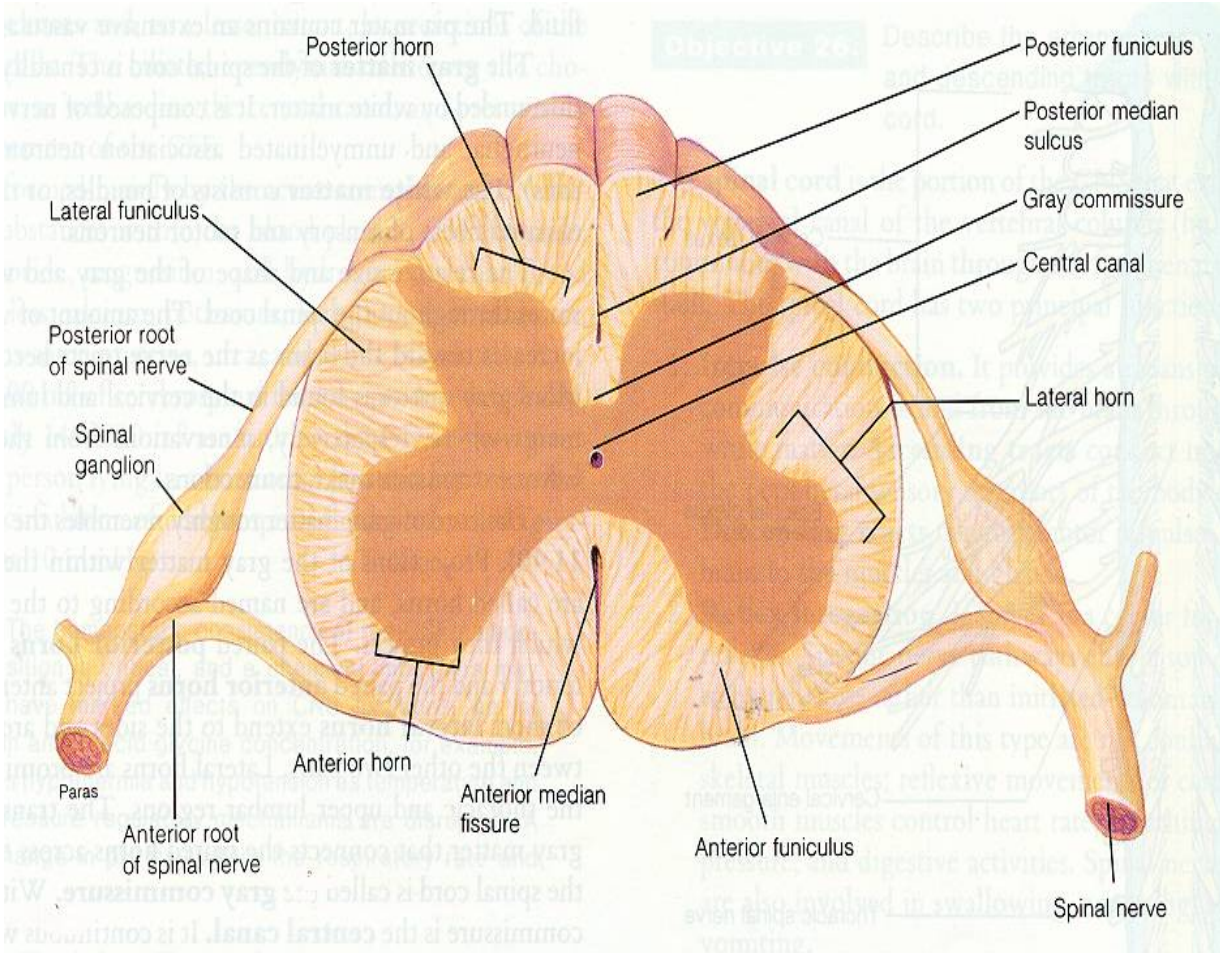
may run long distances up and down the cord or connect parts of the brain with each other.

- ascending tracts- tracts that conduct sensory impulses up the cord.
- descending tracts- tracts that carry motor impulses down the cord.



Grouping of Neural Tissue

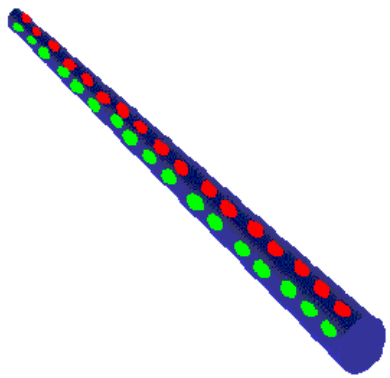
Gray matter- neurons and there cell bodies that do not contain myelin
Ganglia- groups of neuron cell bodies located in the PNS.
Nuclei- groups of neuron cell bodies and dendrites in the CNS.
Horns - the section of the spinal cord where gray matter is located
Columns- groups of white matter tracts in the cord.

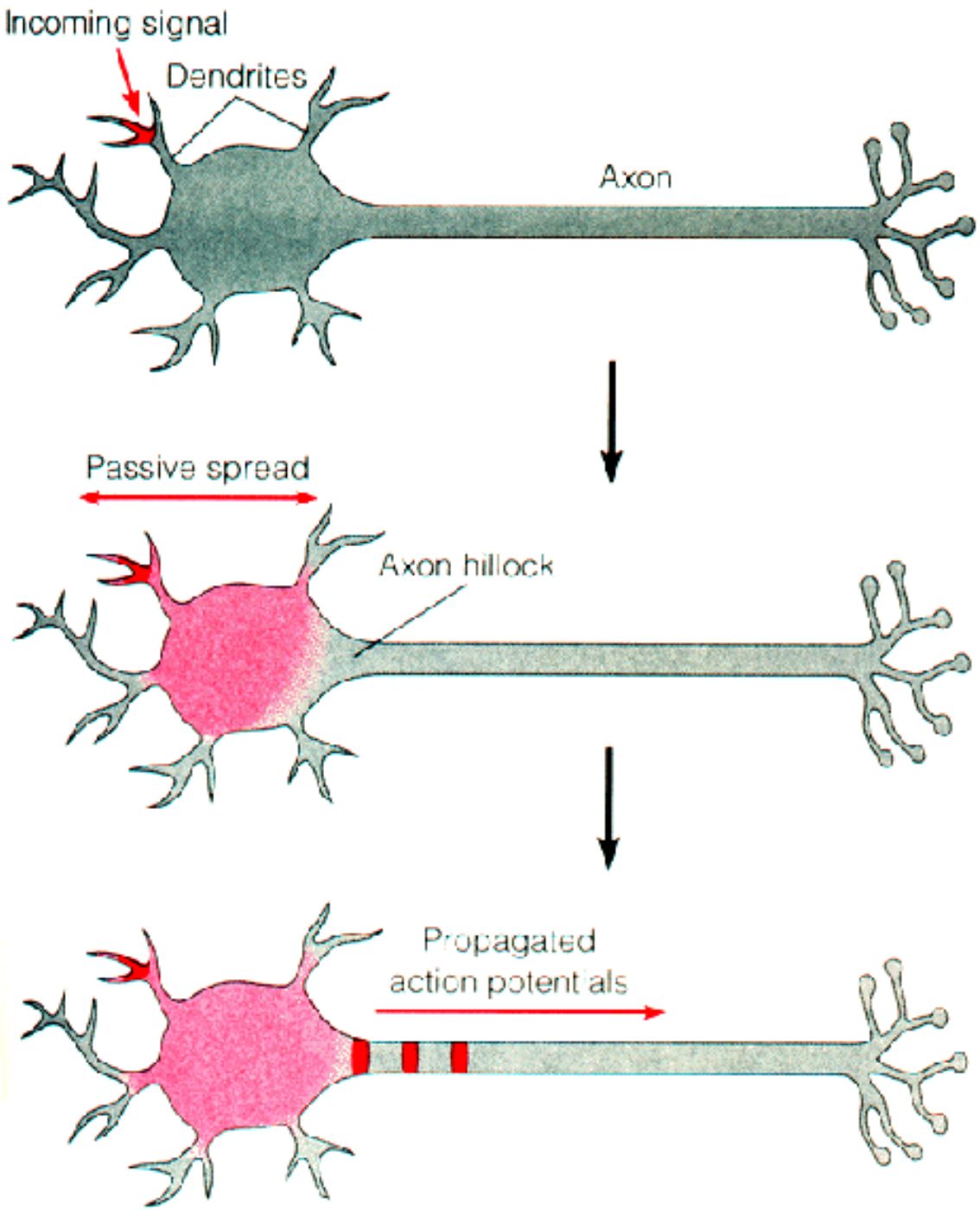


Nerve Impulses

Tiny electric currents that pass along neurons

• result from the movement of ions in and out through the plasma membrane.

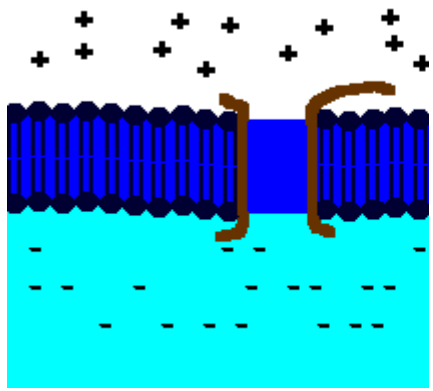



Incoming signal
Dendrites
Axon
Passive spread
Axon hillock
Propagated
action potentials

Nerve Impulses

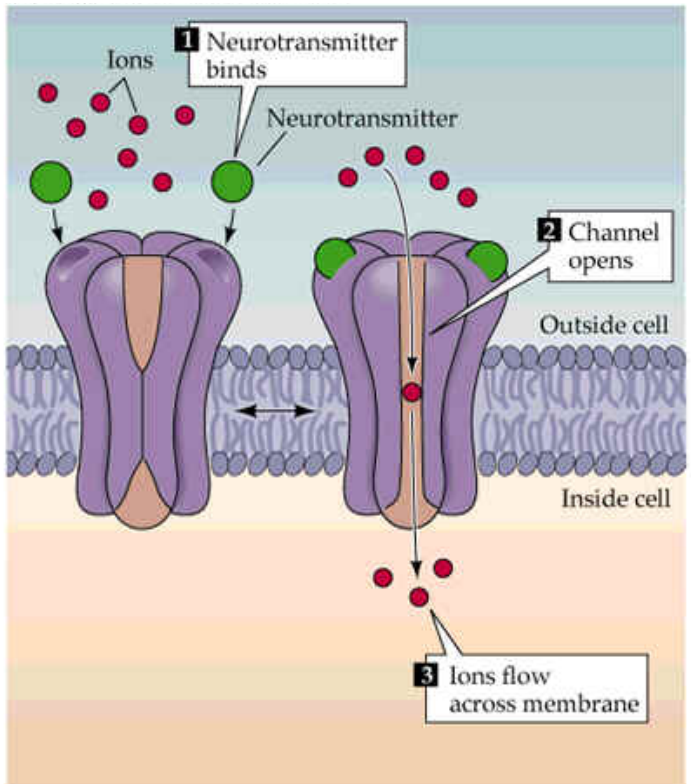
Ion Channels

- the membrane has a variety of ion channels formed by membrane proteins
- most channels are subject to regulation where they are either open (conducting) or closed (nonconducting).



Neural Impulses

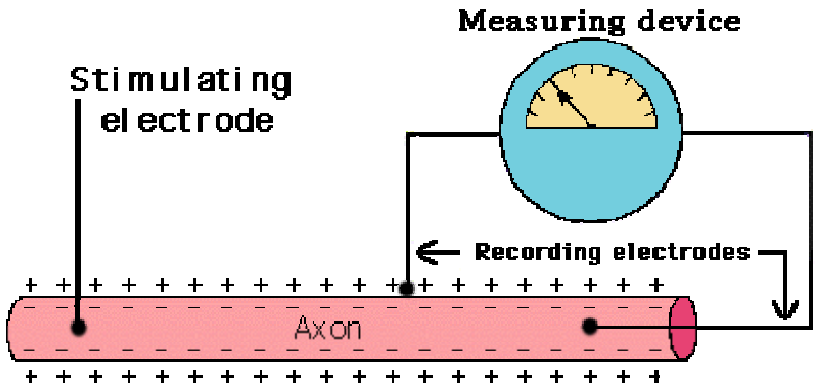
- the protein gate controls the passage of ions by conformational changes in response to various signals.
  - ion concentration across the channel
  - electrical impulses
  - neurotransmitters and hormones



Neural Impulses

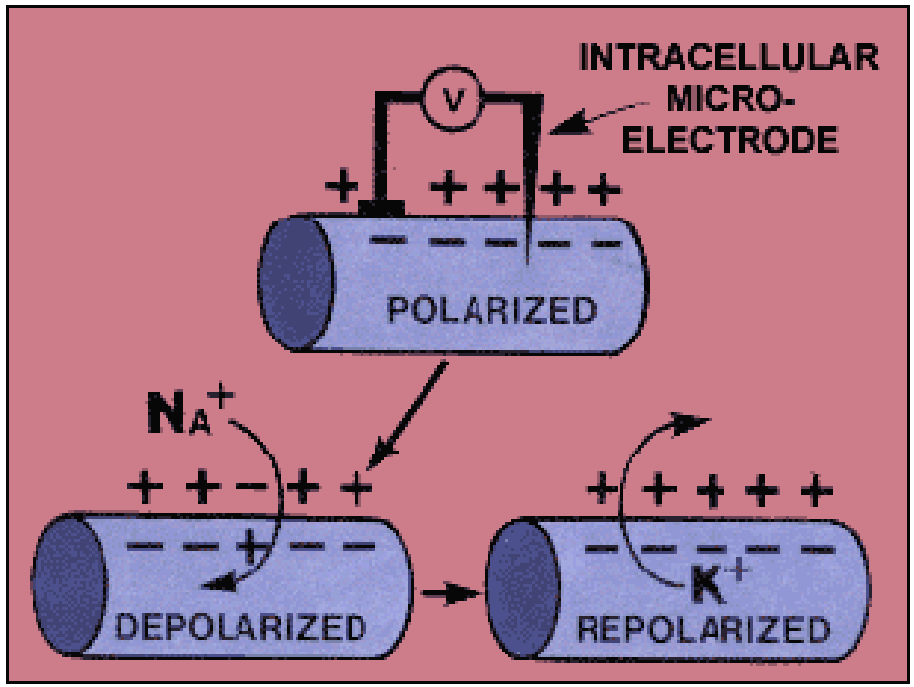
Membrane Potentials

- in a resting membrane their is a difference in the electrical charge between the inside and outside of the neuron.
  - the outside is positive and the inside is negative
  - this occurs because of the differences in the relative concentrations of K+ and negatively charged proteins in side the cell and the Na+ outside the cell.
- the resting charge of a cell at rest is -70 millivolts
- A cell that has a resting membrane potential is said to be **polarized**



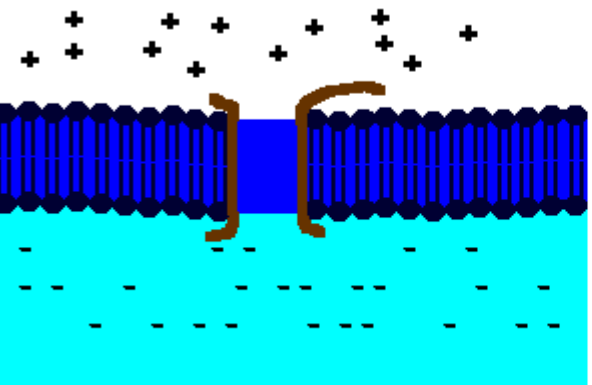
Neural Impulses

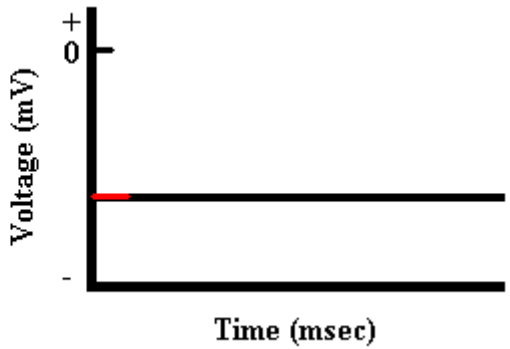
- **Sodium/Potassium pump-** maintains the K+ and Na+ concentrations (thus charge difference or **resting membrane potential**) across the plasma membrane (**Polarized**).

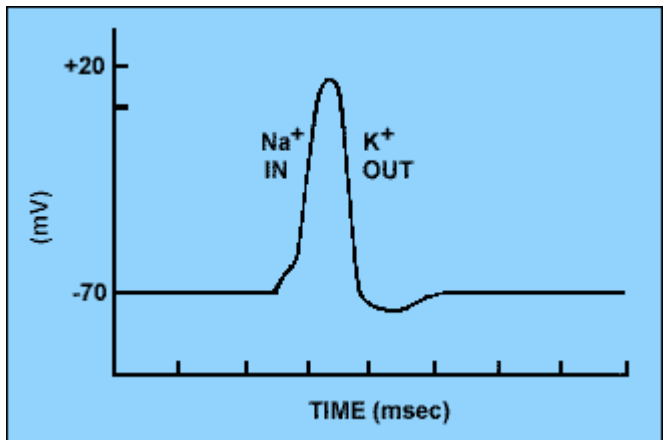


Action Potential

- Is a sequence of rapidly occurring events that decrease and reverse the membrane potential and then eventually restore it to the resting state.
- **Depolarization-** the loss and reversal of polarization due to the rapid opening of sodium ion channels.
- **Repolarization-** the recovery of the resting membrane potential due to the slower opening of potassium ion channels and the closing of sodium ion channels.
- Depolarization and repolarization comprise a nerve impulse and takes only 1 millisecond

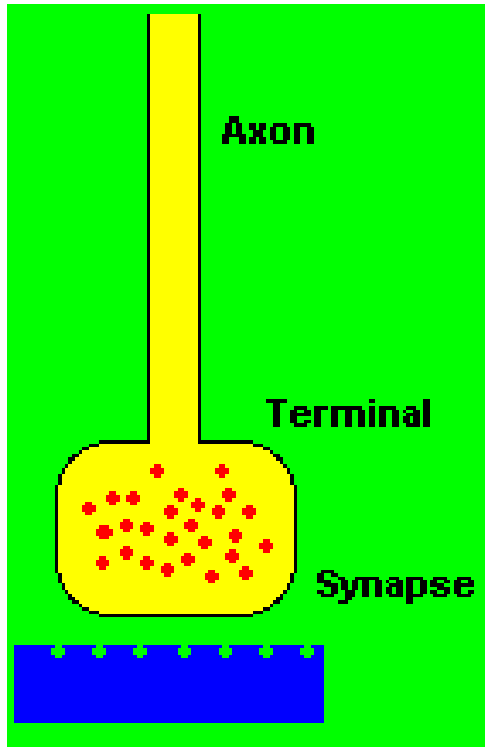


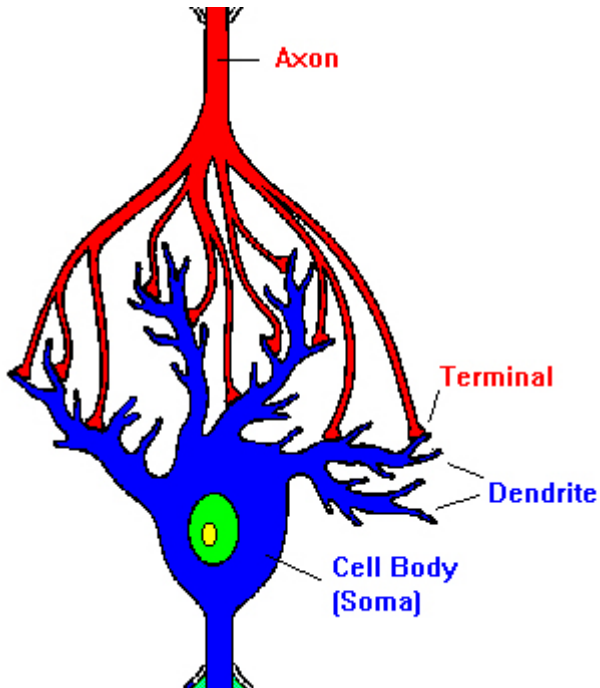




Initiation of a Nerve Impulses

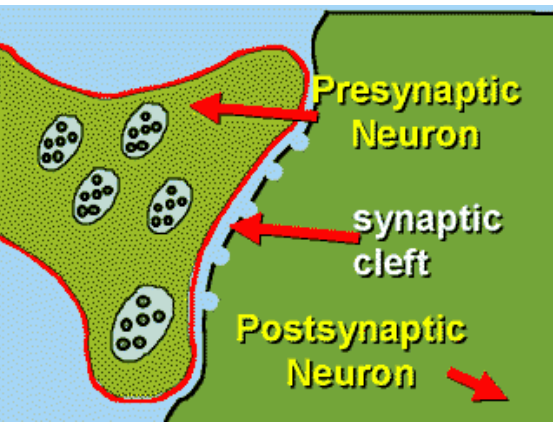
- **Excitability-** the ability of nerve cells to respond to stimuli and convert them into nerve impulses.
- **Stimulus-** anything in the environment capable of changing the membrane resting potential.

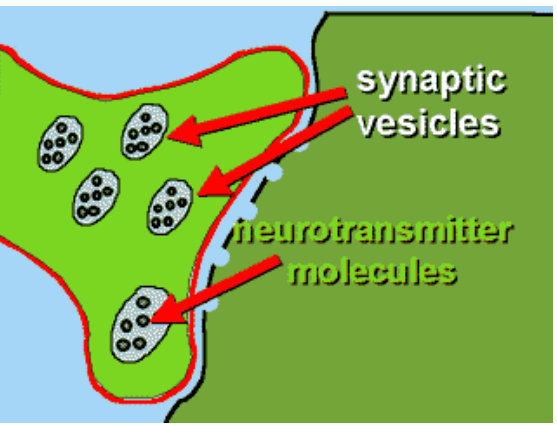


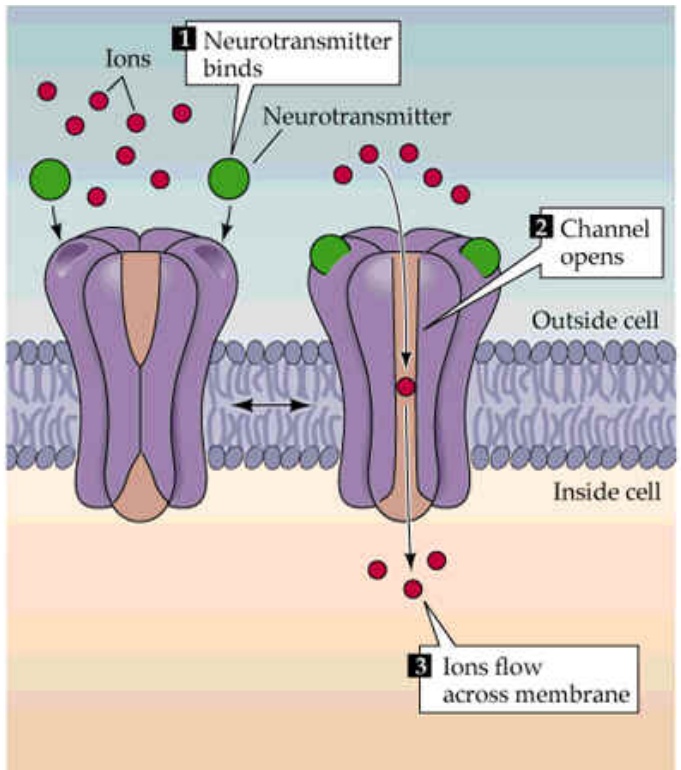


Initiation of Action Potential

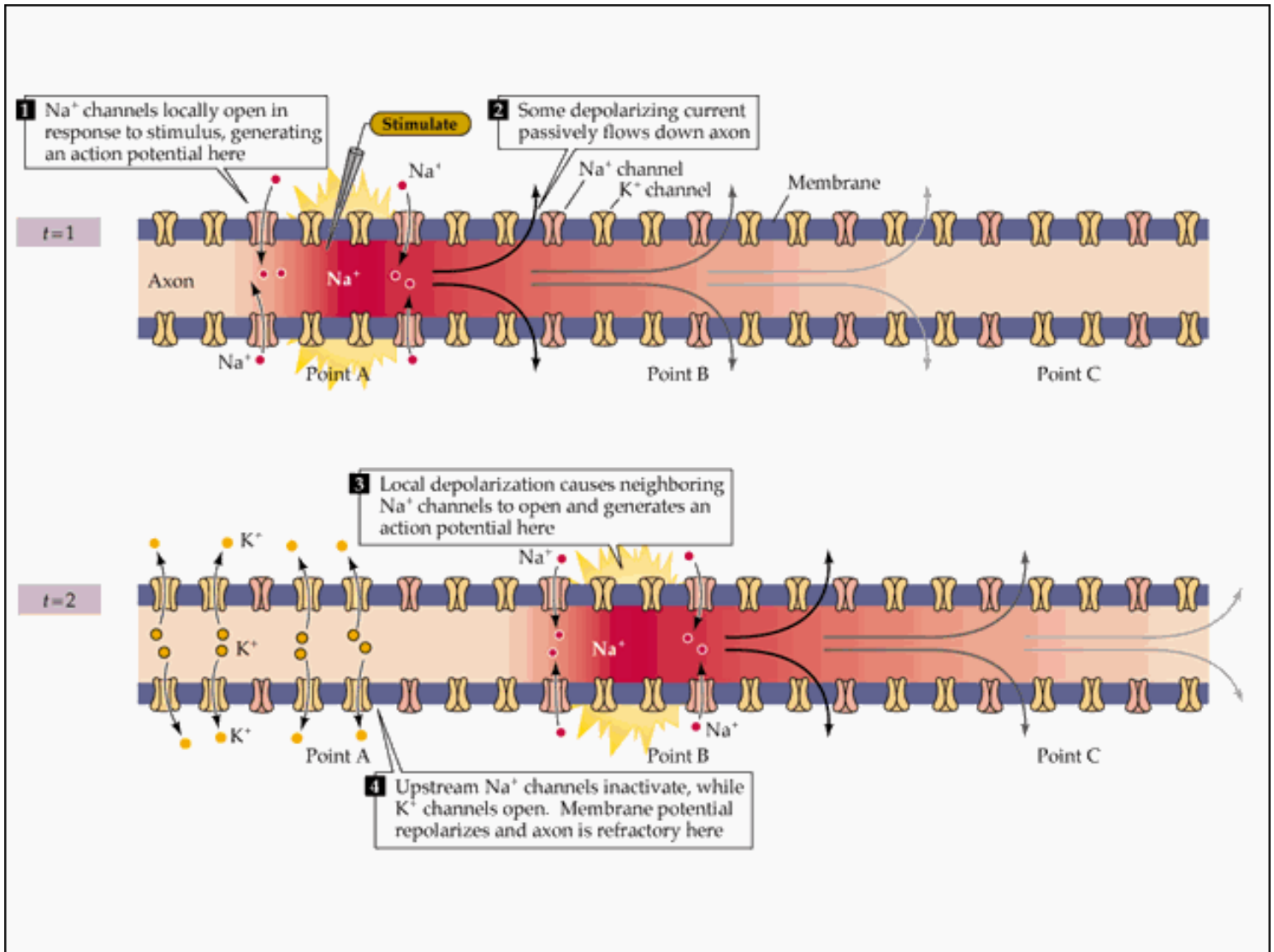
- Caused by the release of neurotransmitter
  - Causes change in membrane potential



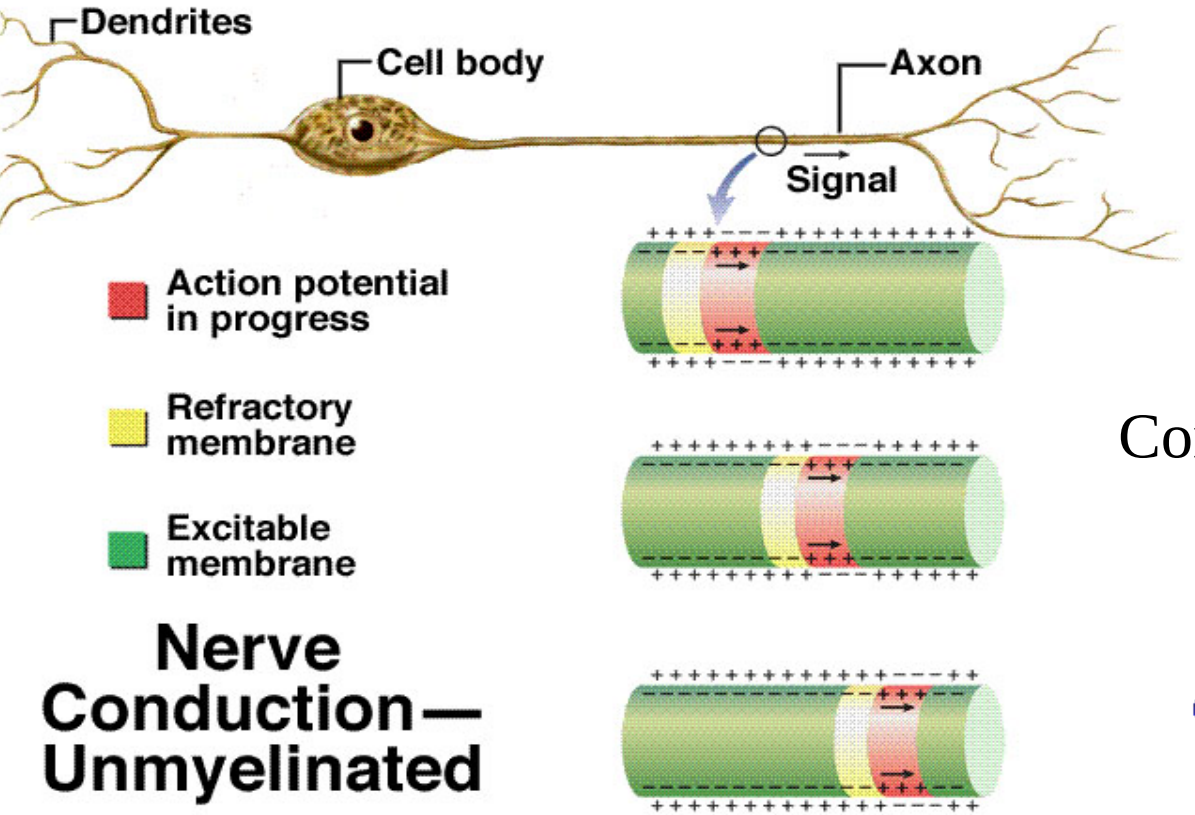




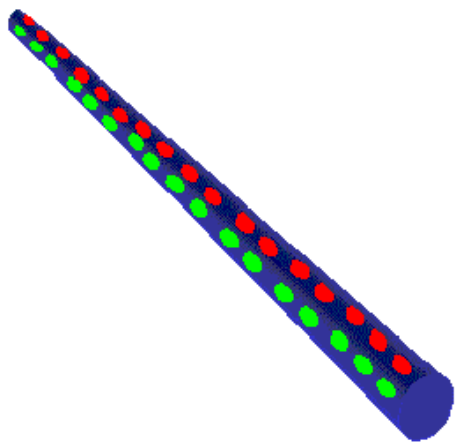
Propagation of Action Potential

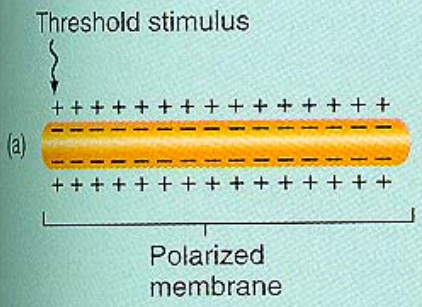


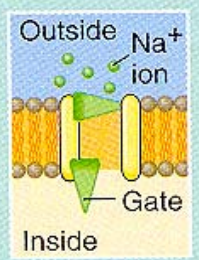
Propagation of Action Potential



Continuous Conduction



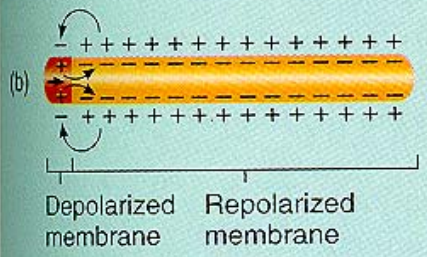


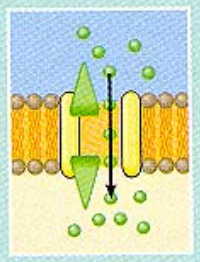


Sodium ion channel is closed

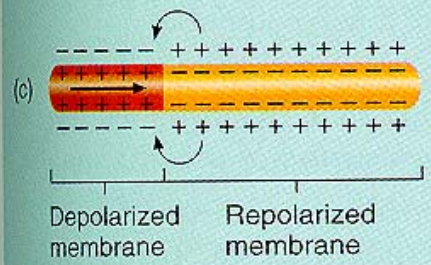
Potassium ion channel is almost closed

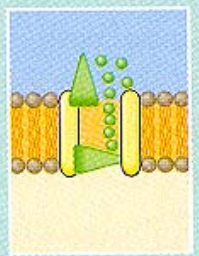
Depolarization
Hyperpolarization
Action Potential
Refractory Period
Threshold Stimulus
Subthreshold Stimulus
All or None Principle
Continuous Conduction



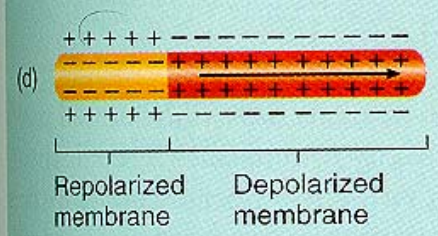


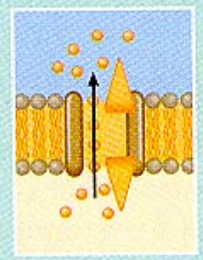
Sodium ion channel is open



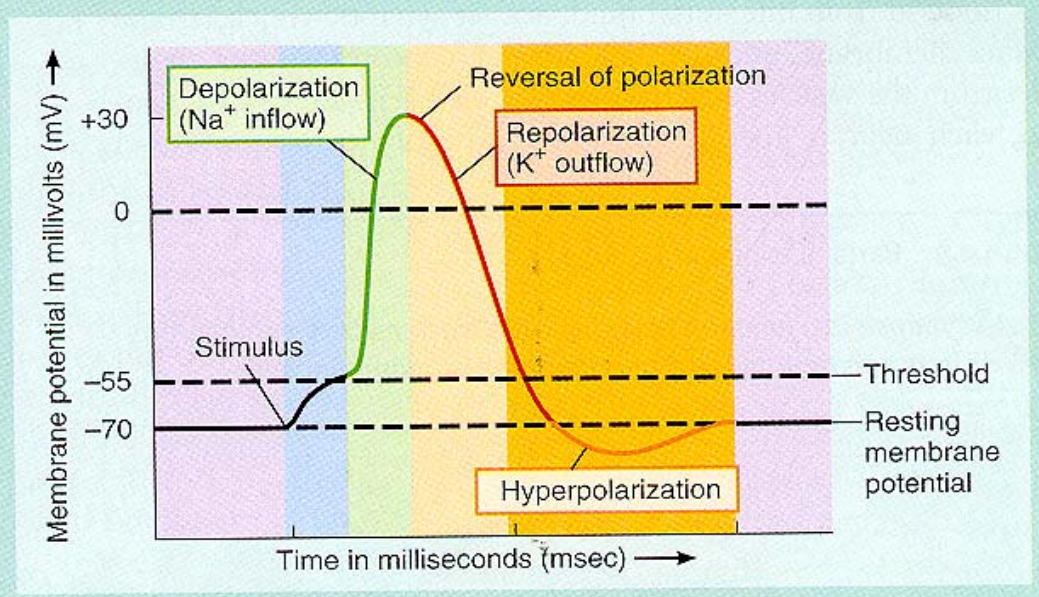


Sodium ion channel is closed





Potassium ion channel is open

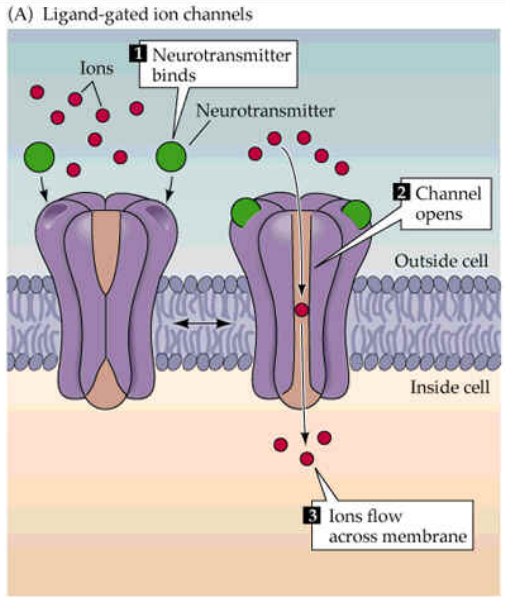


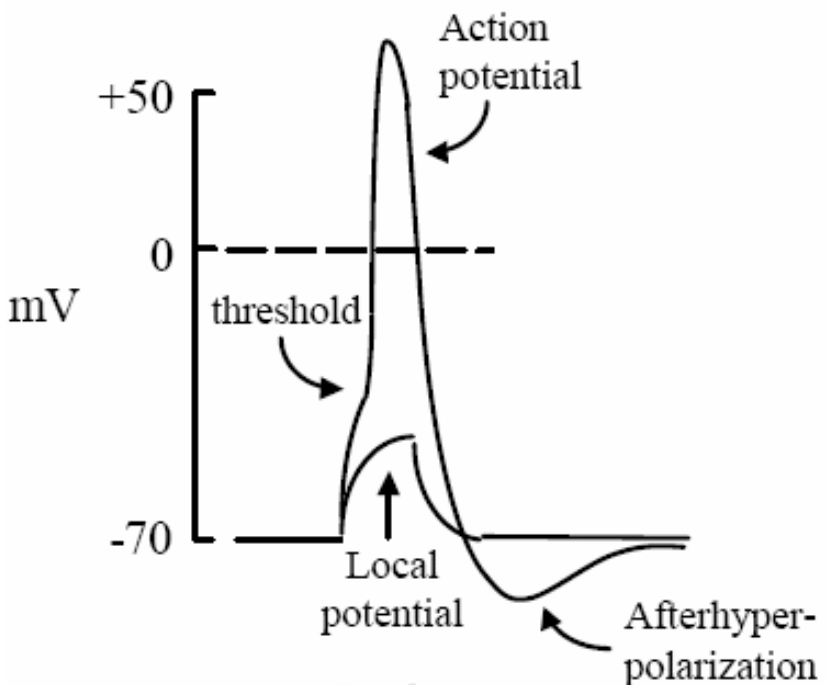
(e)

Local Potentials

- Response of the neuron begins at the dendrites
- Na^+ ligand channels are opened by stimulus causing local depolarization (local potential)

This is not an action potential



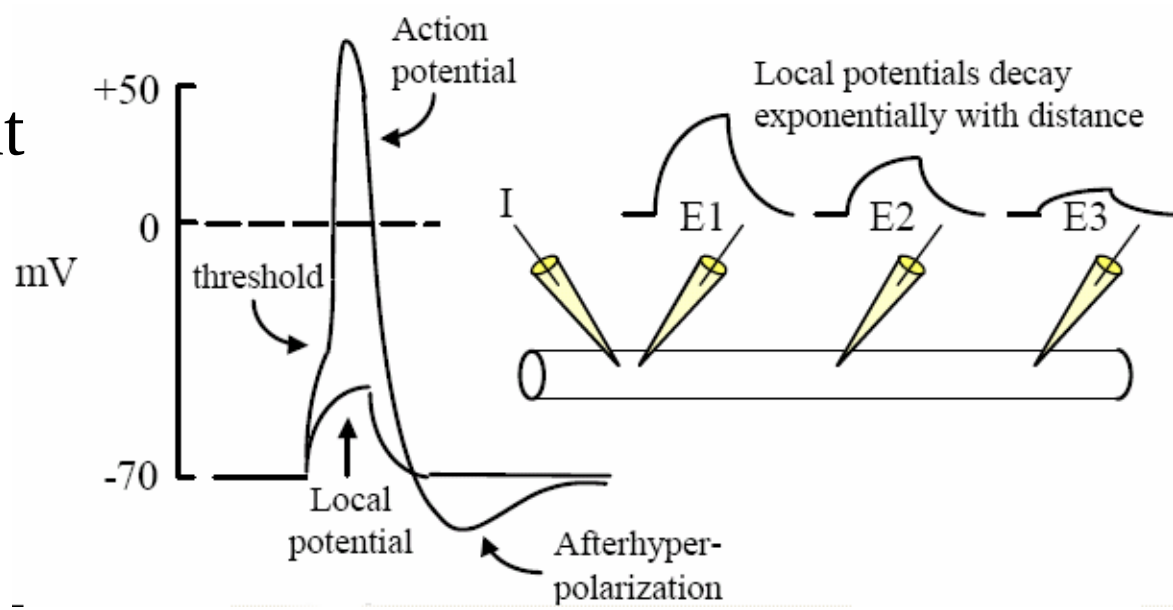


Characteristics that distinguish local potentials from the action potential

- Local potentials are graded- meaning that they vary in magnitude (voltage) according to the strength of the stimulus
  - more intense or prolonged stimulus opens more ion gates than weaker stimulus, thus more Na^+ enters the cell and the voltage changes more than it does a weaker stimulus

Characteristics that distinguish local potentials from the action potential

- Local potentials are decremental- meaning they get weaker as they spread from point of stimulation
  - due to the spreading out of the Na^+ under the plasma membrane



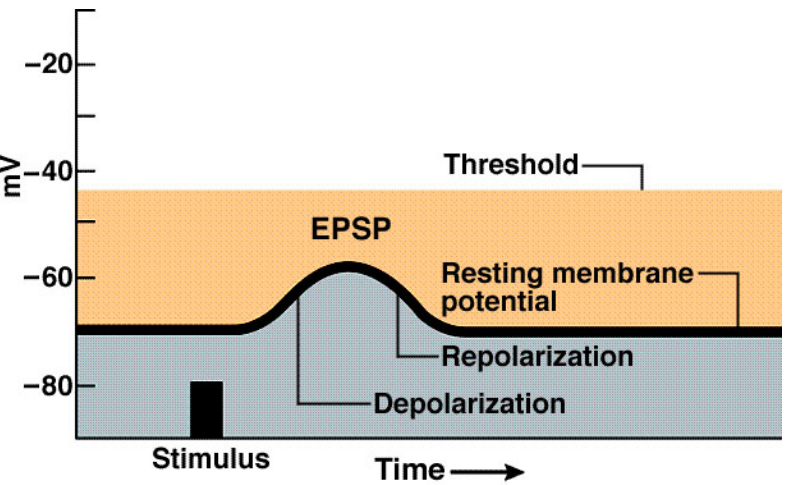
Characteristics that distinguish local potentials from the action potential

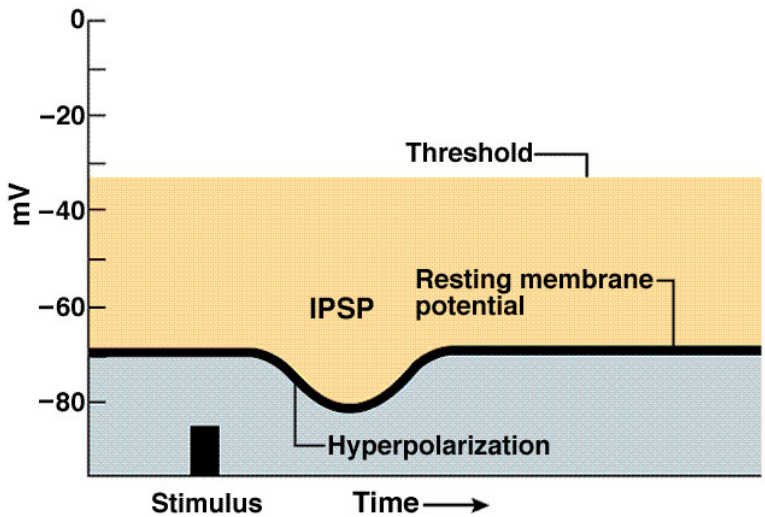
- Local potentials are reversible- meaning if stimulation ceases, K^+ diffusion out of the cell quickly returns the membrane voltage to its resting potential.

Characteristics that distinguish local potentials from the action potential

Local potentials can be either

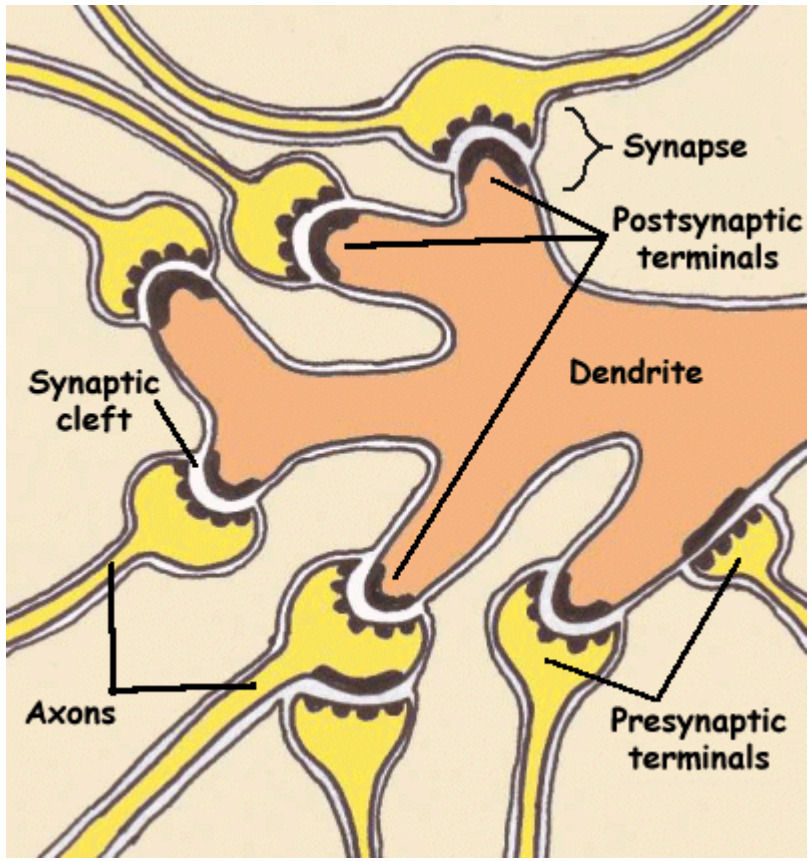
- excitatory- Na^+ flowing in
- inhibitory-
  - produced by opening Cl^- channels to Cl^- to flow in making the inside more negative
  - opening K^+ channels





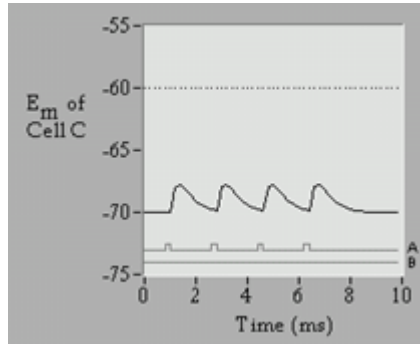
Summation

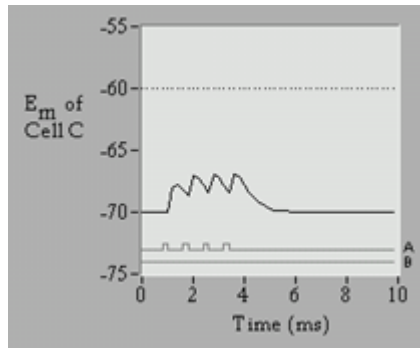
- a neuron receives input from thousands of presynaptic neurons simultaneously of which can be a mixture of IPSP or EPSP
- summation is the process of adding up postsynaptic potentials and responding to their effects

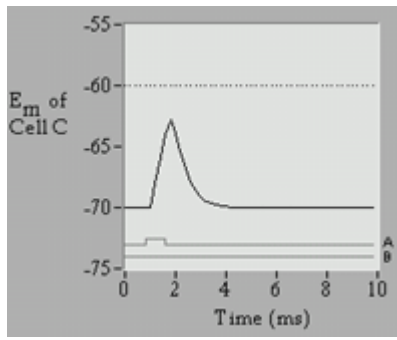


Temporal Summation

- when a single synapse generate EPSP at such short time intervals that each is generated before the previous decays
- This allows the EPSP to add up over time to a threshold that triggers an AP

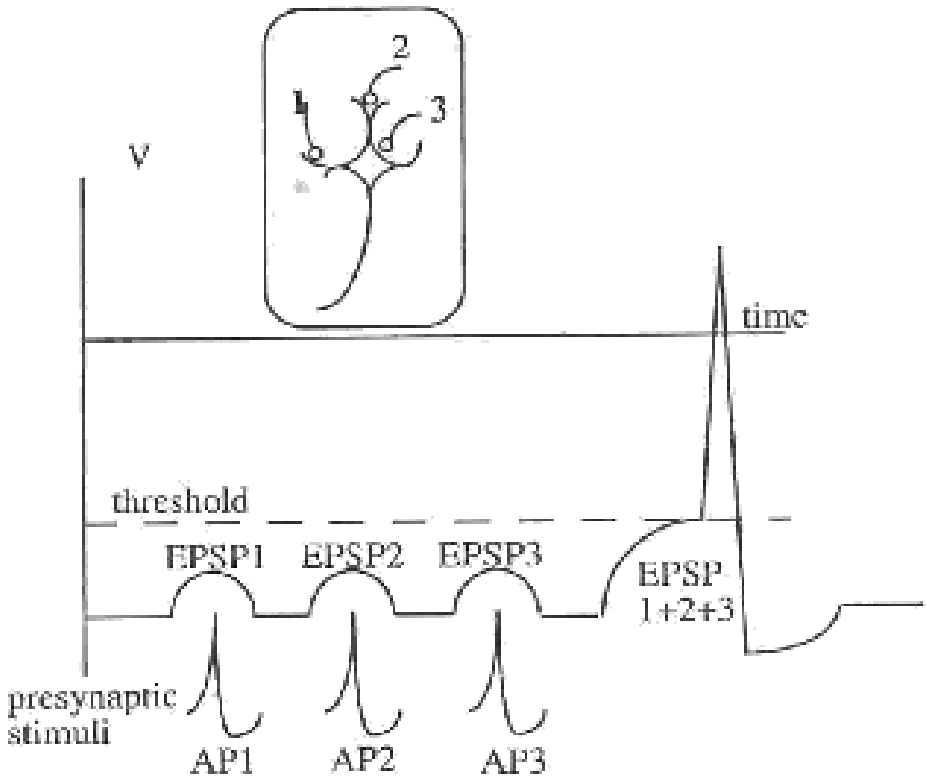






Spatial Summation

- when EPSP's from several different synapses add up to threshold at the axon hillock
  - any one synapse may admit only a moderate amount of Na+ but several synapses acting together admit enough to reach threshold



Facilitation

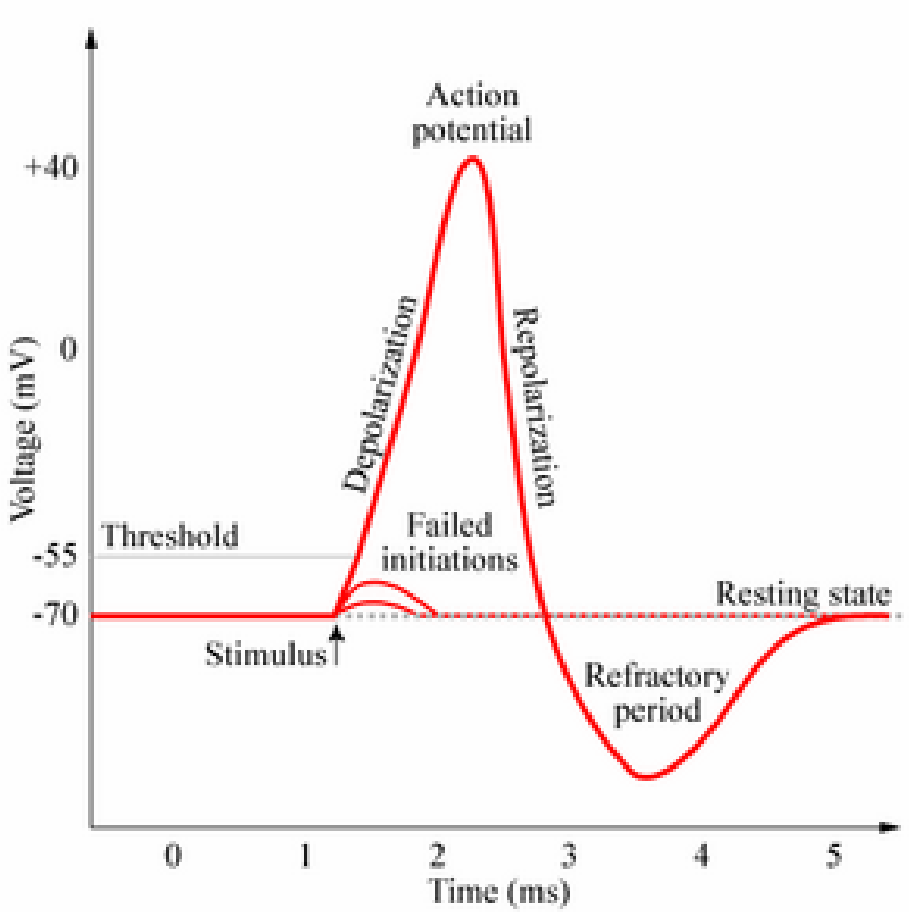
- a process in which one neuron enhances the effect on another one
  - ex. one neuron acting alone is not enough to cause a AP but when combined with the effects of another neuron, then it maybe enough to cause firing.

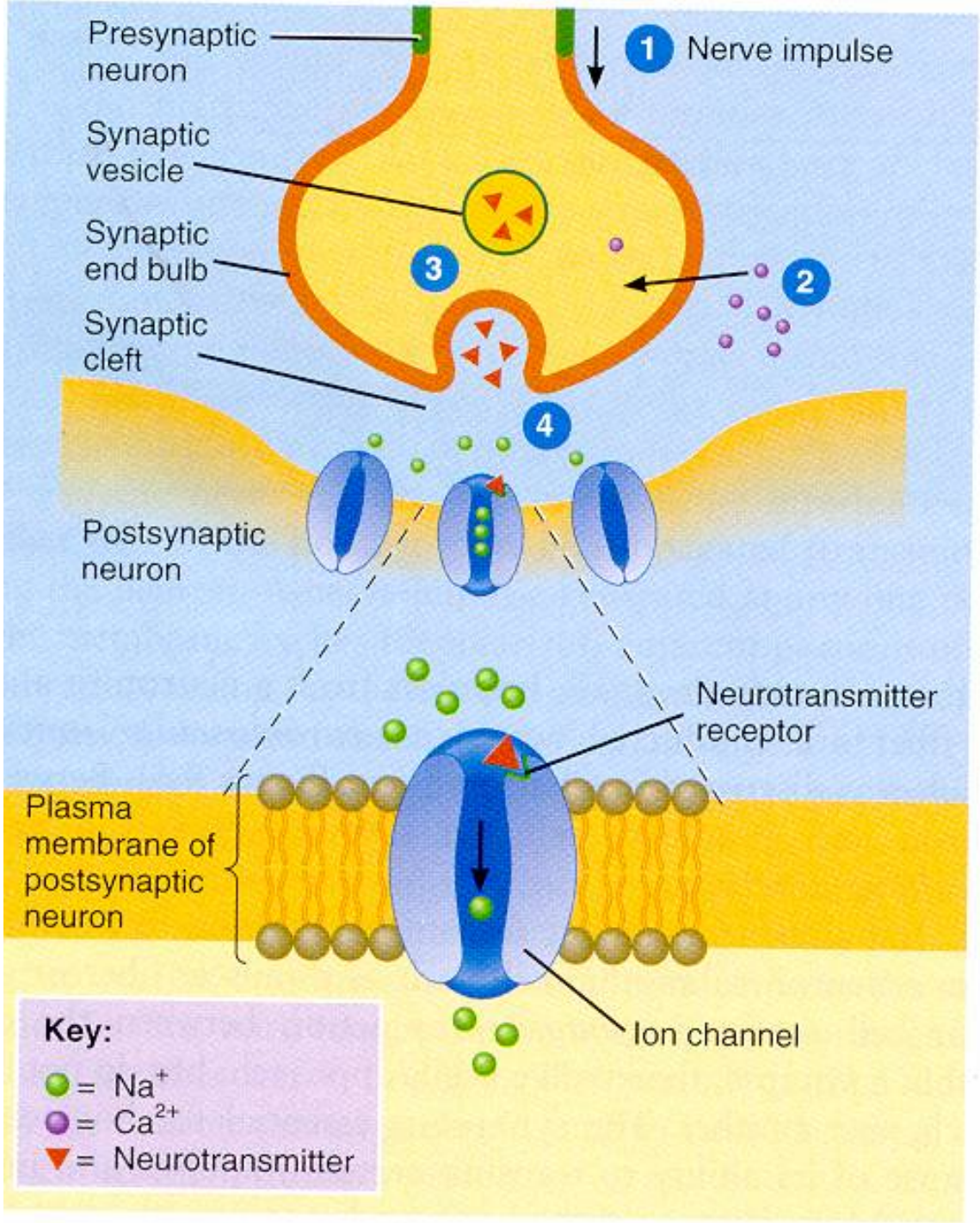
Presynaptic Inhibition

- the opposite of facilitation: when one presynaptic neuron suppresses another one

Action Potential

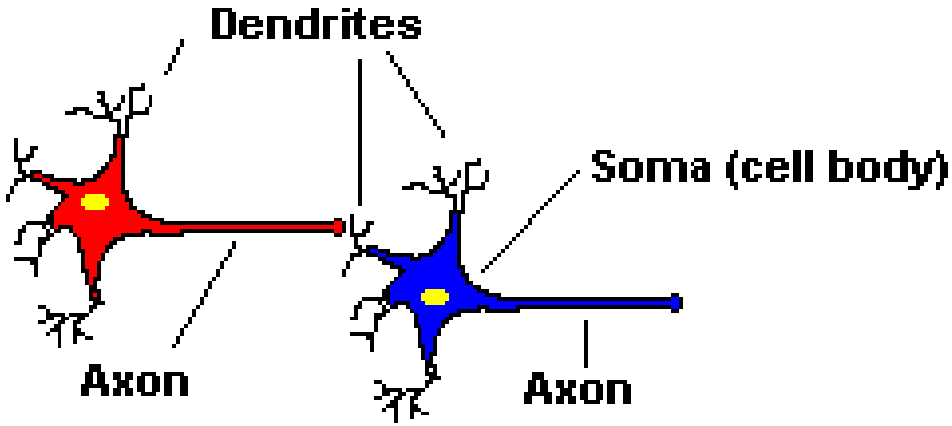
- A more dramatic change produced by voltage-gated ion channels in the plasma membrane
  - occurs where there is a high enough density of channels
    - soma 50-75 channels per square micrometer
    - trigger zone- 350-500 gates per square micrometer
  - if excitatory local potential spreads to the trigger zone and is strong enough when it arrives (reaching threshold), it can open Na^+ gates and generate an AP
- Threshold- minimum level of depolarization to cause an AP

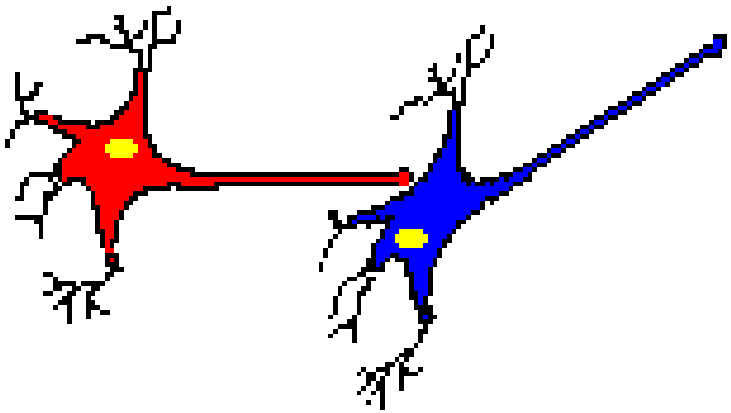


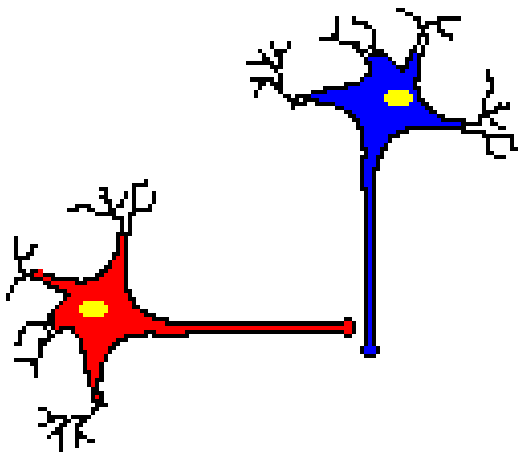


inhibitory

AP in muscle





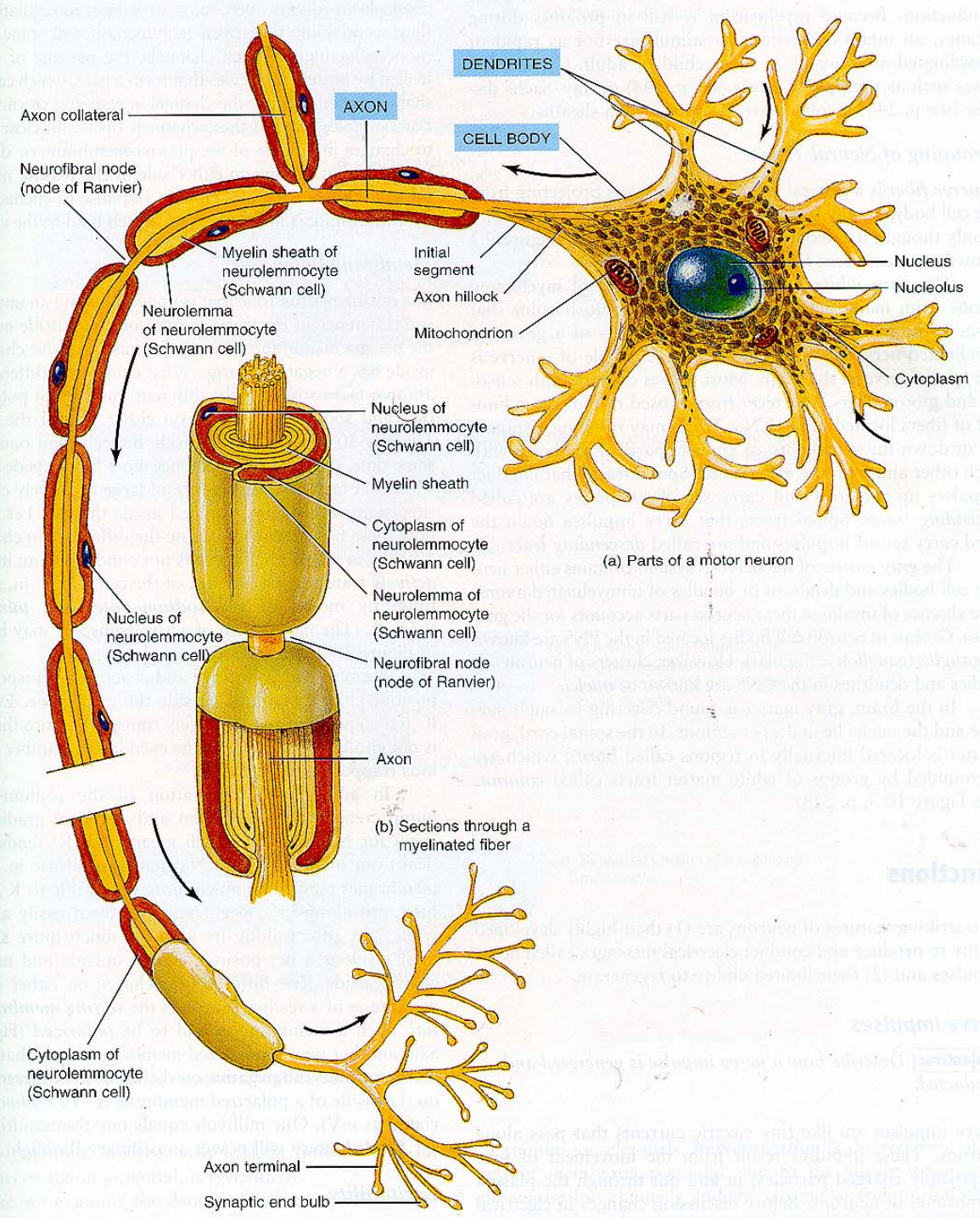


Synapses

Axodendritic

Axosomatic

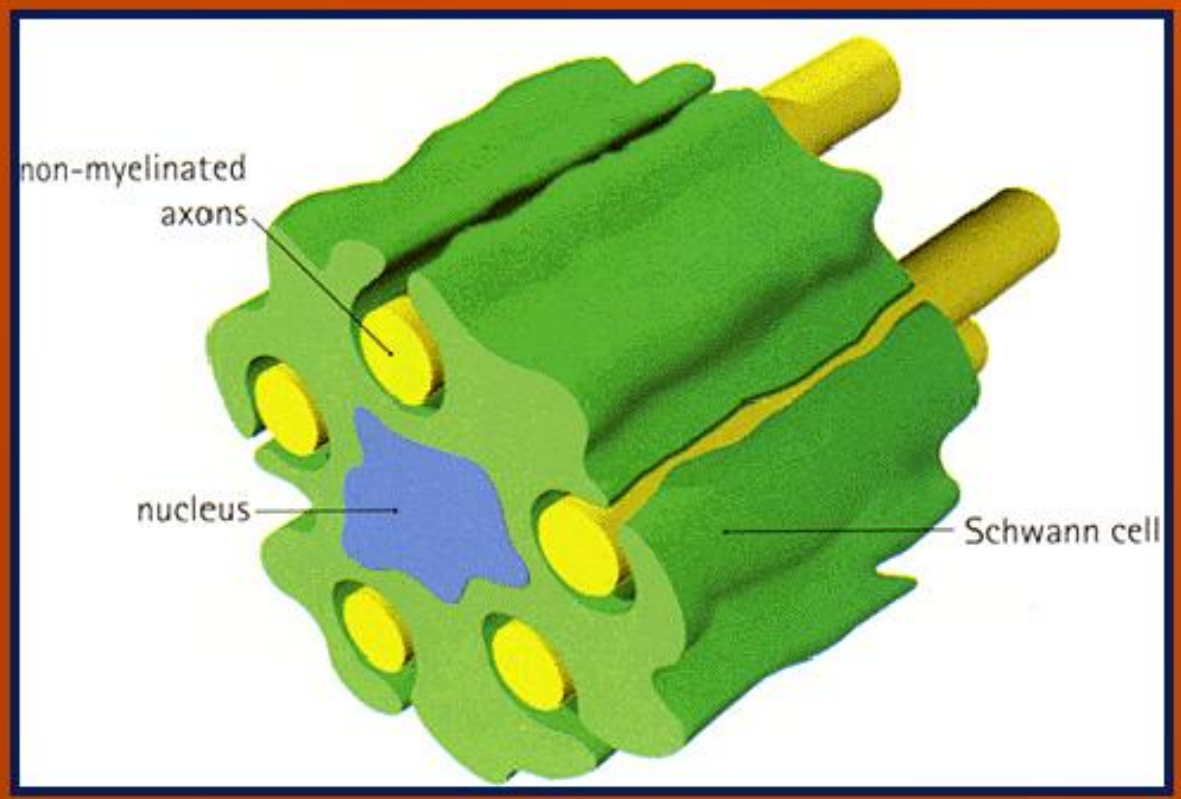
Axoaxonic



- Nodes of Ranvier- gaps between myelinated segments
- Internodes- segments of myelin between nodes
- initial segment- section of nerve between axon hillock and first glial cell
- trigger zone- segment where nerve signal is initiated (initial segment and axon hillock

PNS Unmyelinated Fibers

Schwann Cell: supporting non-myelinated nerves



- No wrapper of myelin
- Just support
  - multiple axons in this case

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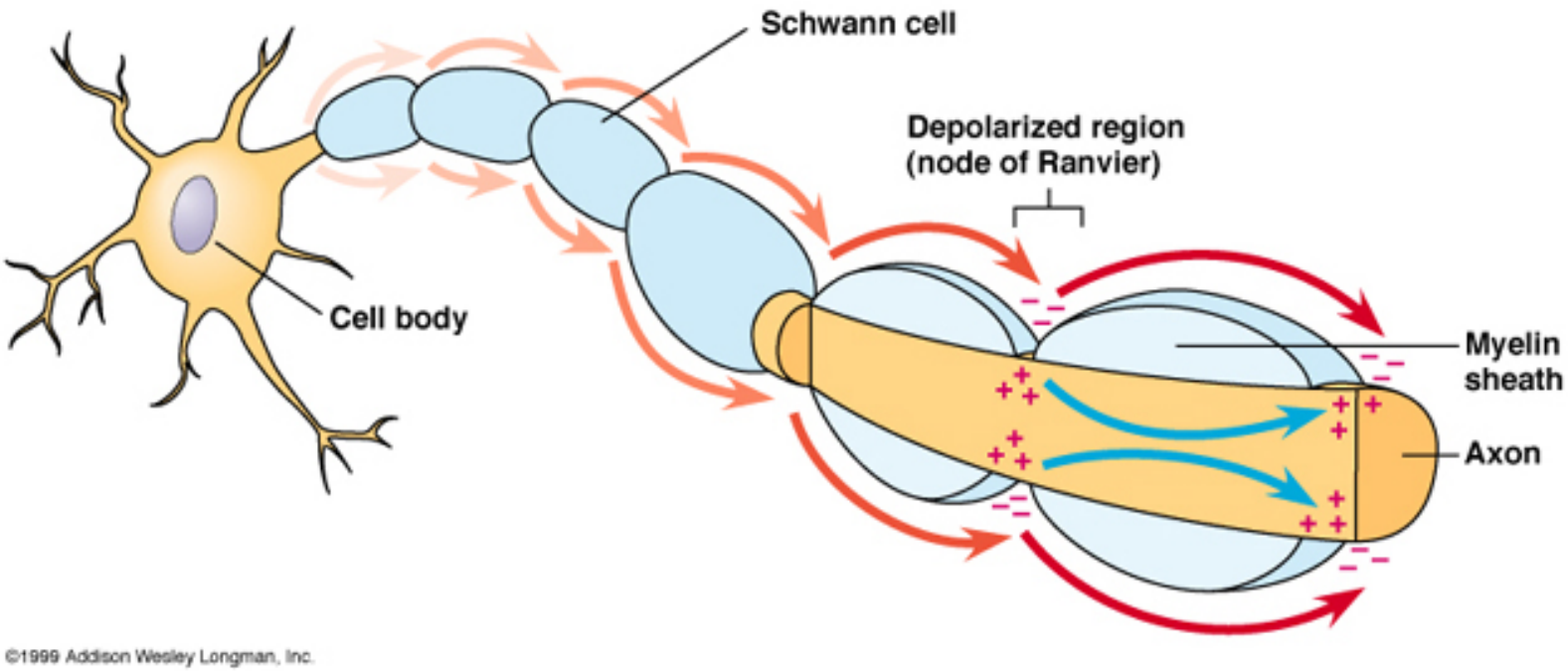
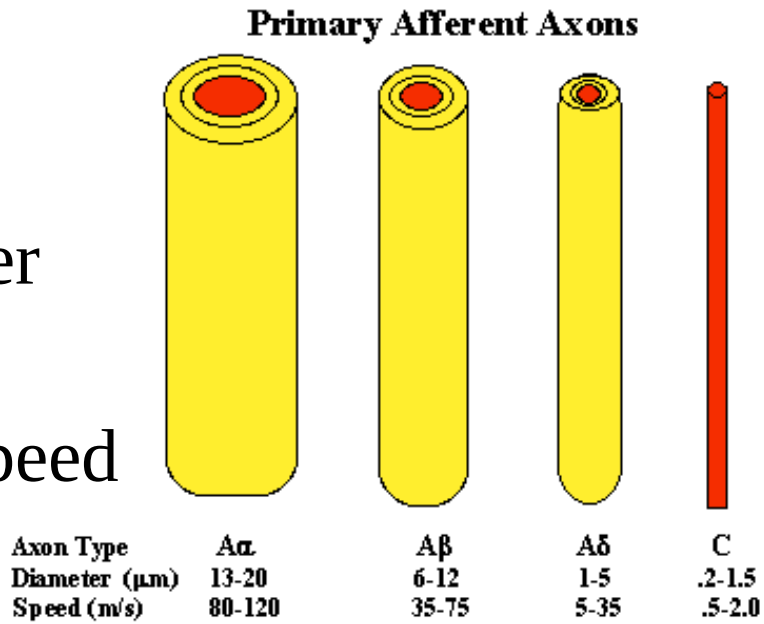
Neural Conduction in Mylinated Fibers: Saltatory Conduction



Speed of Nerve Impulses

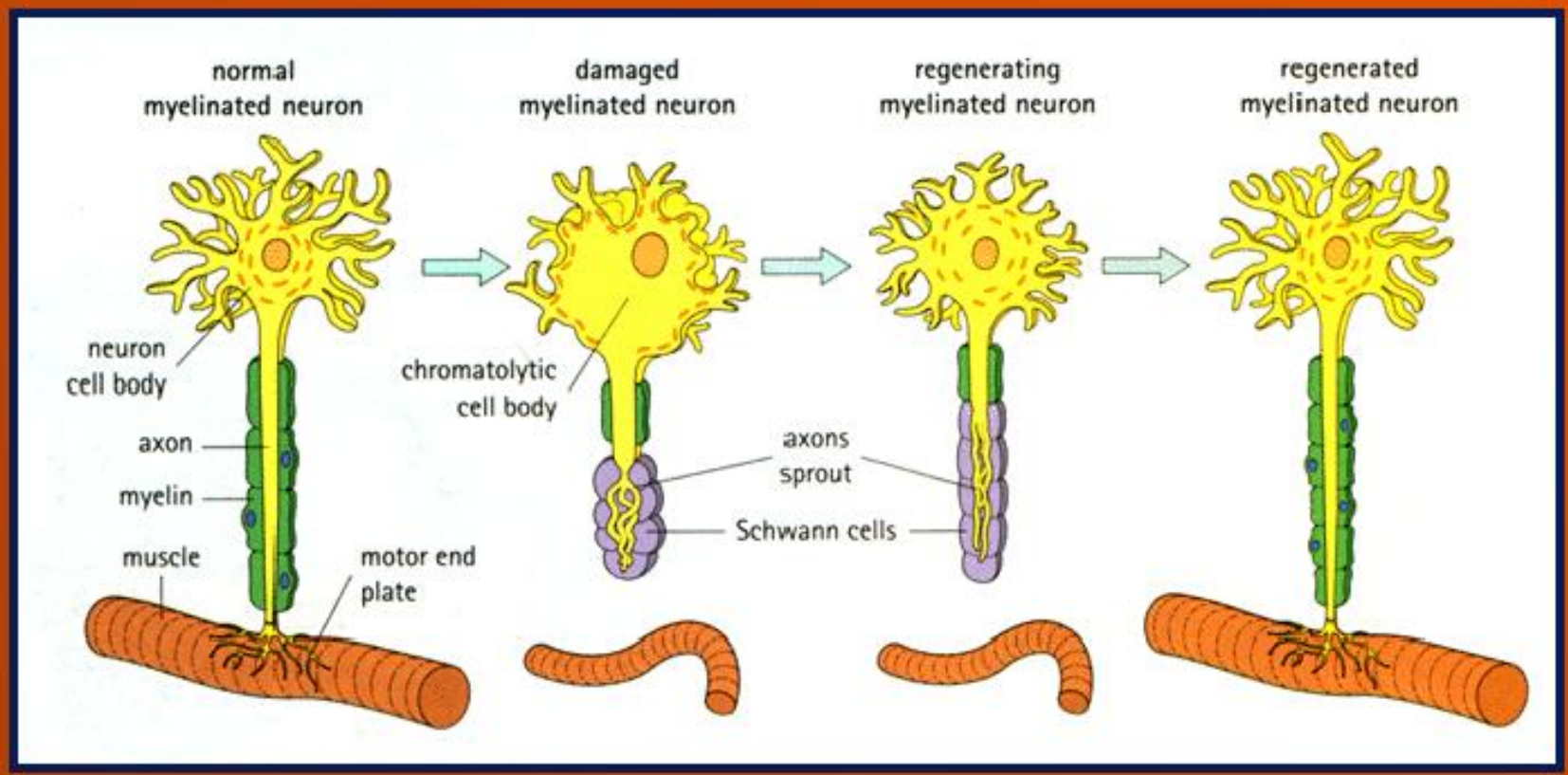
The speed of a nerve impulse is determined by

- temperature- speed is faster at warmer temperatures
- fiber diameter- speed is faster in larger diameter fibers due to larger surface area for conduction
- presence or absence of myelin- speed is faster in myelinated fibers (saltatory conduction)
  - large fibers are myelinated
  - smaller fibers are unmyelinated



Nerve Repair

A regeneration tube or guidance channel is necessary for nerve regrowth and is formed by the neurilemma and endoneurium



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Neurotransmitter Criteria

- The chemical must be produced within a neuron.
- The chemical must be found within a neuron.
- When a neuron is stimulated (depolarized), a neuron must release the chemical.
- When a chemical is released, it must act on a post-synaptic receptor and cause a biological effect (alter the physiology of that cell).
- After a chemical is released, it must be inactivated. Inactivation can be through a reuptake mechanism or by an enzyme that stops the action of the chemical.
- If the chemical is applied on the post-synaptic membrane, it should have the same effect as when it is released by a neuron.

Types of Neurotransmitters

Three major categories

- Acetylcholine
- Amino Acids
  - GABA
  - Glycine
  - Aspartic acid
  - Glutamic acid
- Biogenic amines (monoamines)
  - Catecholamines
    - epinephrine
    - norepinephrine
    - dopamine
  - Serotonin
  - Hisamine
- Neuropeptides

-Some neurotransmitters are excitatory and some are inhibitory

-for some the effect depends on what kind of receptor the postsynaptic cell has

-some are ligand gated ion channels and some act through the second messenger systems

Synapse

Excitatory Cholinergic synapse

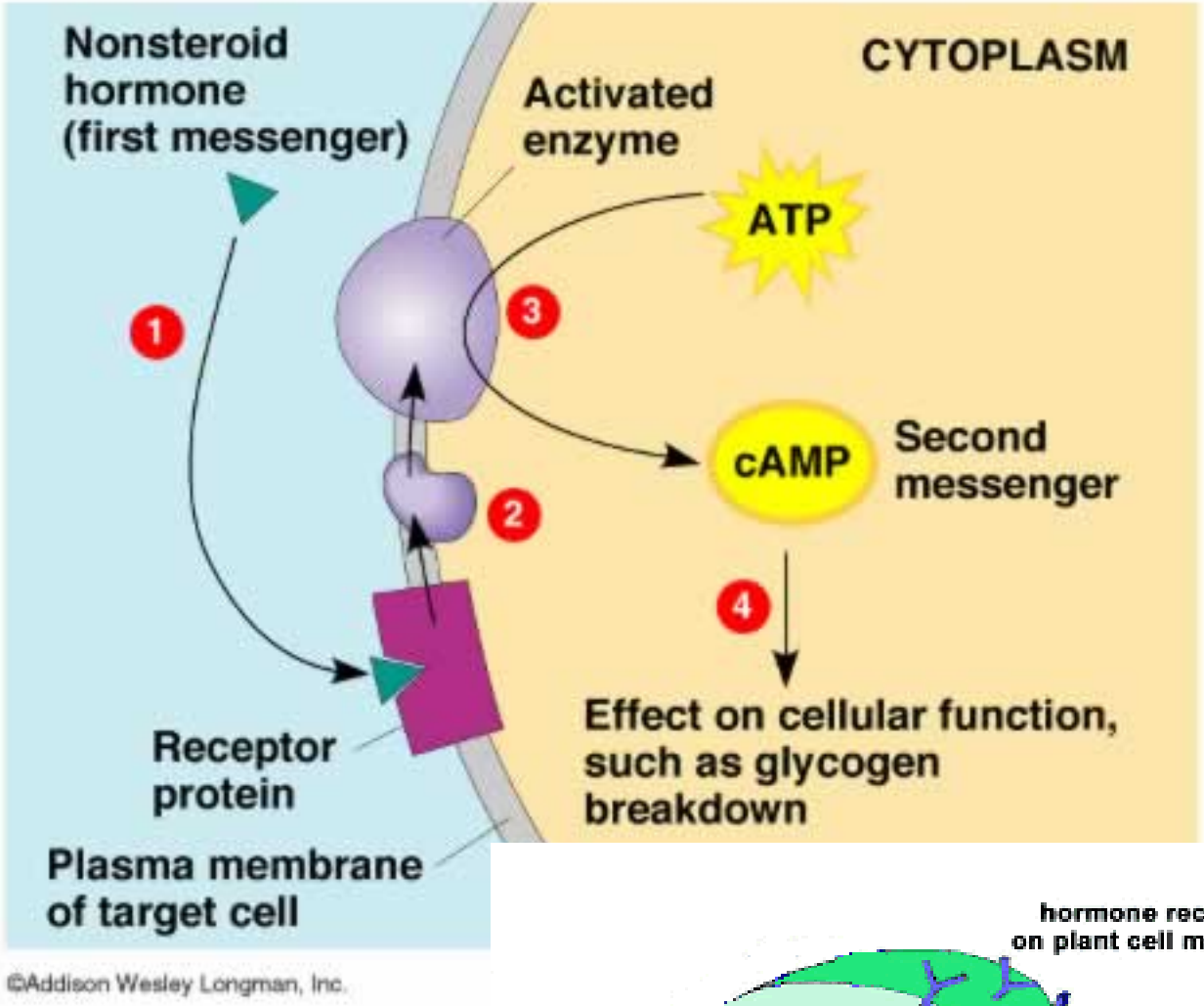
- employs acetylcholine as its neurotransmitter (can be excitatory or inhibitory)
  - opens Na+ channels

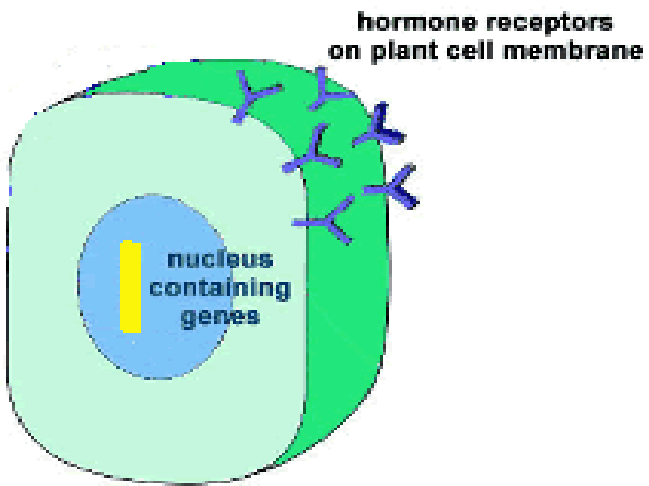
Inhibitory GABA-ergic synapse

- opens Cl- channels causing a hyperpolarization

Adrenergic excitatory synapse

- employs norepinephrine
- acts through second messenger systems such as cyclic AMP
- the receptor is not an ion gate but an integral protein associated with G protein



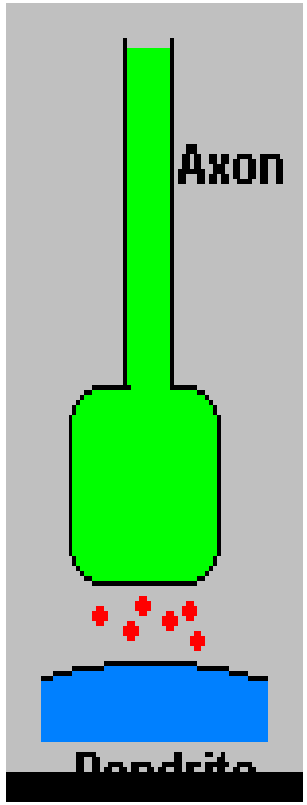


1. the binding of NE activates the G protein
2. which activates adenylate cyclase
3. which converts ATP to cAMP
4. cAMP can have multiple effects such as stimulating the synthesis of new enzymes

Inactivation of Neurotransmitters

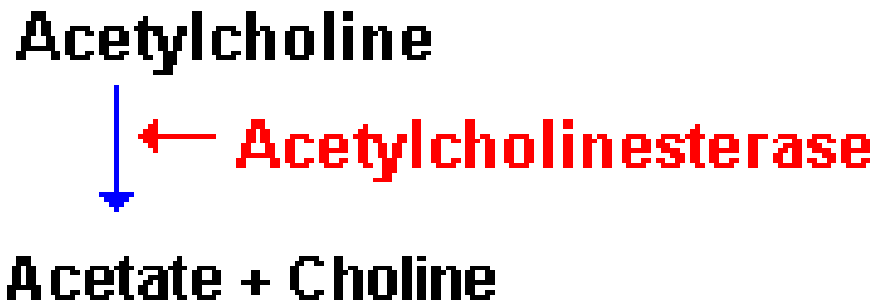
The action of neurotransmitters can be stopped by four different mechanisms

1. Diffusion: the neurotransmitter drifts away, out of the synaptic cleft where it can no longer act on a receptor.



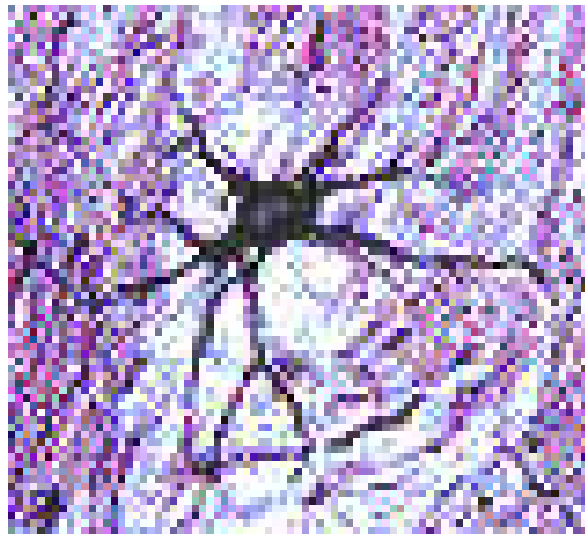
Inactivation of Neurotransmitters

- 2. Enzymatic degradation (deactivation): a specific enzyme changes the structure of the neurotransmitter so it is not recognized by the receptor. For example, acetylcholinesterase is the enzyme that breaks acetylcholine into choline and acetate.



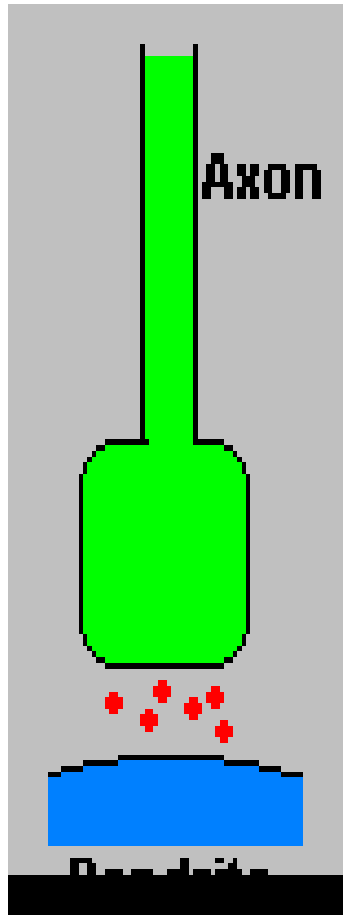
Inactivation of Neurotransmitters

- 3. Glial cells:
  astrocytes remove
  neurotransmitters from
  the synaptic cleft.



Inactivation of Neurotransmitters

- 4. Reuptake: the whole neurotransmitter molecule is taken back into the axon terminal that released it by endocytosis and then is broken down by an enzyme called monoamine oxidase (MNO
  - some antidepressant drugs work by inhibiting MAO
- This is a common way the action of norepinephrine, dopamine and serotonin is stopped...these neurotransmitters are removed from the synaptic cleft so they cannot bind to receptors.



Summary of the major biochemical effects that drugs may have at the

- synapse:
- Precursor compounds
- Synthesis blockade
- Transmitter depletion
- Prevention of release
- Receptor inhibition
- Mimicking
- Inactivation blockade
- Reuptake blockade
- False transmitters (+)
- False transmitters (-)
- Conduction blockade